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NEWS WWW CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 07:24:30 ON 28 APR 2005

=> HBV (L) treatment
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=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'CAPLUS' ENTERED AT 07:25:05 ON 28 APR 2005
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FILE COVERS 1907 - 28 Apr 2005 VOL 142 ISS 18
FILE LAST UPDATED: 27 Apr 2005 (20050427/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> HBV (l) treatment
7681 HBV
53 HBVS
7697 HBV
(HBV OR HBVS)
2006213 TREATMENT
185728 TREATMENTS
2105955 TREATMENT
(TREATMENT OR TREATMENTS)
L1 1357 HBV (L) TREATMENT

=> nucleoside
43410 NUCLEOSIDE
29795 NUCLEOSIDES
L2 54411 NUCLEOSIDE
(NUCLEOSIDE OR NUCLEOSIDES)

=> L2 and L1
L3 218 L2 AND L1

=> Interferon
65244 INTERFERON
67532 INTERFERONS
L4 82016 INTERFERON
(INTERFERON OR INTERFERONS)

=> L3 and l4
L5 58 L3 AND L4

=> fibrosis and L5
28868 FIBROSIS
L6 2 FIBROSIS AND L5

=> D L6 IBIB ABS 1-2

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:126760 CAPLUS

DOCUMENT NUMBER: 139:270294
TITLE: Lamivudine therapy in renal allograft recipients with hepatitis B virus infection
AUTHOR(S): Tsang, W. K.; Tong, K. L.; Chan, H. W. H.
CORPORATE SOURCE: Department of Medicine and Geriatrics, Division of Nephrology, Princess Margaret Hospital, Hong Kong, Peop. Rep. China
SOURCE: Transplantation Proceedings (2003), 35(1), 278-279
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Renal allograft recipients, due to heavy immunosuppression, are at risk of developing more aggressive hepatitis, cirrhosis, and, less frequently, hepatocellular carcinoma resulting in higher liver-related morbidity and mortality rates. Interferon .alpha. has been reported to be assocd. with high incidence of acute rejection in renal transplant patients. Lamivudine is a new cytidine nucleoside analog that inhibits DNA synthesis through interference with the reverse transcriptase activity of hepatitis B virus (HBV). It has been shown to be effective in suppressing HBV replication in immunocompetent patients with HBV infection. Preliminary studies show that lamivudine is useful in treating chronic hepatitis B in renal transplant patients. We studied the efficacy and safety of lamivudine in Asian renal allograft recipients with HBV infection. Lamivudine was found to be safe and very effective in the suppression of HBV replication, normalization of alanine aminotransferase (ALT), enhancement of HBeAg seroconversion, and seldomly, eradication of HBV. It can be a useful therapeutic option for HBV infection in renal transplant recipients with abnormal ALT. Effects of long-term treatment and/or combination antiviral therapy on viral replication, fibrosis, and hepatocellular carcinoma incidence should be evaluated.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:576865 CAPLUS
DOCUMENT NUMBER: 129:159923
TITLE: Therapy of viral hepatitis
AUTHOR(S): Hoofnagle, Jay H.
CORPORATE SOURCE: Liver Diseases Section, Digestive Diseases Branch, Natl. Inst. Diabetes Digestive Kidney Diseases, Natl. Inst. Health, Bethesda, MD, 20892, USA
SOURCE: Digestion (1998), 59(5), 563-578

CODEN: DIGEBW; ISSN: 0012-2823
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 136 refs. is given. Worldwide hviral hepatitis is the most common cause of jaundice, chronic liver disease cirrhosis and hepatocellular carcinoma. While important advances have been made in prevention of viral hepatitis, therapy of this disease remains unsatisfactory. There are no specific therapies of proven benefit for acute hepatitis, although use of alpha-interferon during the acute phase of hepatitis C may result in a decrease in the rate of chronicity. For chronic viral hepatitis, alpha-interferon has been widely used, but is expensive, poorly tolerated and limited in effectiveness. New antiviral agents and use of combinations of antivirals are now being evaluated and promise to provide a therapy that is effective in the majority of patients. The currently recommended therapy of chronic hepatitis B is a 4- to 6-mo course of alpha-interferon in doses of 5-10 million units three times a week; a regimen that results in sustained clearance of hepatitis B virus (HBV) DNA and hepatitis B e antigen (HBeAg) from serum in approx. one-third and a loss of hepatitis B surface antigen (HBsAg) in one-tenth of patients. Long-term follow-up of patients who respond to interferon treatment with clearance of HBeAg indicate that the majority ultimately clear HBsAg as well and have continued remission in the liver disease, although low levels of HBV DNA can commonly be detected in liver tissue. Better therapies of hepatitis B are needed. Recently, several oral "second-generation" nucleoside analogs have been developed that have potent activity against HBV. The best studied is lamivudine (3-thiacytidine) which results in marked inhibition of HBV DNA levels and improvement in serum aminotransferases and hepatic histol. in the majority of patients. When stopped, however, most patients relapse and the shortcomings of long-term therapy have been the development of viral resistance in up to one-quarter of patients within a year and a higher percentage with more prolonged therapy. Future approaches of therapy of promise for hepatitis B are combinations of lamivudine with interferon and other antiviral nucleoside analogs. The currently recommended therapy of chronic hepatitis C is a 12- to 18-mo course of alpha interferon in doses of 3 million units three times a week: a regimen that results in sustained clearance of hepatitis C virus (HCV) RNA in approx. 20% of patients. Sustained responses have been assocd. with marked improvements in hepatic histol. and long-term studies indicate that the majority of patients remain free of virus in serum and liver, suggesting a "cure" of infection. Responses to interferon correlate to some degree with clin. and virol. features, including young age, absence of hepatic fibrosis, low levels of HCV RNA in serum and HCV genotypes 2 and

3. Most recently, combinations of alpha interferon and ribavirin, an oral nucleoside analog, have been evaluated and shown to increase the sustained response rate to 30 - 40%. Better therapies are still needed, as the majority of patients with hepatitis C do not have a sustained response to therapy. Extensive research on the mol. structure of HCV indicates several potential means of inhibition of viral replication, including use of protease and helicase inhibitions. What is most needed to advance the field of therapeutics in hepatitis C is development of animal models and cell culture systems with which to study this important viral cause of liver disease.

```
=> lamivudine and HBV (s) treatment
       2575 LAMIVUDINE
       7681 HBV
         53 HBVS
       7697 HBV
            (HBV OR HBVS)
    2006213 TREATMENT
     185728 TREATMENTS
    2105955 TREATMENT
            (TREATMENT OR TREATMENTS)
        829 HBV (S) TREATMENT
L7      342 LAMIVUDINE AND HBV (S) TREATMENT

=> "coronary virus"
      57778 "CORONARY"
        223 "CORONARIES"
      57844 "CORONARY"
            ("CORONARY" OR "CORONARIES")
     317840 "VIRUS"
      67819 "VIRUSES"
     329474 "VIRUS"
            ("VIRUS" OR "VIRUSES")
L8        1 "CORONARY VIRUS"
            ("CORONARY"(W)"VIRUS")

=> coronavirus
       2883 CORONAVIRUS
        647 CORONAVIRUSES
L9     2966 CORONAVIRUS
            (CORONAVIRUS OR CORONAVIRUSES)

=> SARS
L10    1986 SARS
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=> L9 and L10
L11 950 L9 AND L10

=> fibrosis
L12 28868 FIBROSIS

=> L11 and L12
L13 5 L11 AND L12

=> interferon and L11
65244 INTERFERON
67532 INTERFERONS
82016 INTERFERON
(INTERFERON OR INTERFERONS)
L14 66 INTERFERON AND L11

=> nucleoside and L11
43410 NUCLEOSIDE
29795 NUCLEOSIDES
54411 NUCLEOSIDE
(NUCLEOSIDE OR NUCLEOSIDES)
L15 15 NUCLEOSIDE AND L11

=> L14 and L15
L16 6 L14 AND L15

=> L16 and L13
L17 1 L16 AND L13

=> D L17 IBIB ABS

L17 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:930930 CAPLUS
DOCUMENT NUMBER: 141:343458
TITLE: Treatment of HMPV infections with ribavirin
INVENTOR(S): Maertzdorf, Jeroen; Simon, James Henry Matthew
PATENT ASSIGNEE(S): Vironovative B.V., Neth.
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 1473037 A1 20041103 EP 2003-76299 20030502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
WO 2004096241 A1 20041111 WO 2004-NL293 20040503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: EP 2003-76299 A 20030502
AB The invention relates to antiviral agents and compns. comprising such agents to treat and/or prevent respiratory diseases, in particular those caused by human metapneumovirus. Provided is a method for treating or preventing respiratory tract infections in a subject infected with a mammalian MPV, said method comprising administering a nucleoside analog, preferably Ribavirin or a deriv. thereof, to said subject, and use of said nucleoside analog for the manuf. of a medicament for treating or preventing respiratory tract infections in a subject infected with a mammalian MPV.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L16 IBIB ABS 1-6

L16 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:238669 CAPLUS
DOCUMENT NUMBER: 142:291330
TITLE: Targeted delivery of antiviral compounds through hemoglobin bioconjugates
INVENTOR(S): Adamson, J. Gordon; Bell, David; Ng, Nancy; Biessels, Pieter
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 32 pp., Cont.-in-part of U.S. Ser. No. 231,062.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005059576	A1	20050317	US 2004-846597	20040517
CA 2236344	AA	19991030	CA 1998-2236344	19980430
US 6479637	B1	20021112	US 1999-302351	19990430
US 2003013642	A1	20030116	US 2002-231062	20020830

PRIORITY APPLN. INFO.: CA 1998-2236344 A 19980430
US 1999-302351 A1 19990430
US 2002-231062 A2 20020830
US 2003-470445P P 20030515
US 2003-513575P P 20031024

AB This invention relates to targeted delivery of anti-viral compds. through protein bioconjugation. More particularly, it relates to an anti-viral compd. conjugated to a protein, such as Hb and to a method of treating a viral infection using said conjugate. The invention also provides a method of targeted drug delivery of an anti-viral nucleoside analog to macrophages, cells comprising a Hb receptor and to CD163 bearing cells.

L16 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1124599 CAPLUS
DOCUMENT NUMBER: 142:49199
TITLE: Compositions and methods for treating coronavirus infection and SARS with interferons
INVENTOR(S): Blatt, Lawrence M.
PATENT ASSIGNEE(S): Intermune, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110392	A2	20041223	WO 2004-US7819	20040312

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005002901 A1 20050106 US 2004-814701 20040330

PRIORITY APPLN. INFO.: US 2003-459783P P 20030401

AB The present invention provides methods of treating a coronavirus infection, and methods of reducing viral load, or reducing the time to viral clearance, or reducing morbidity or mortality in the clin. outcomes, in patients suffering from a coronavirus infection. The present invention further provides methods of reducing the risk that an individual will develop a pathol. coronavirus infection, that has clin. sequelae. The present invention further provides methods of reducing the risk that an individual will develop SARS. The present invention further provides methods of treating SARS. The methods generally involve administering a therapeutically effective amt. of a Type I or Type III interferon receptor agonist and/or a Type II interferon receptor agonist for the treatment of a coronavirus infection.

L16 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1087826 CAPLUS

DOCUMENT NUMBER: 142:92001

TITLE: Ribavirin and interferon-.beta. synergistically inhibit SARS-associated coronavirus replication in animal and human cell lines

AUTHOR(S): Morgenstern, Birgit; Michaelis, Martin; Baer, Patrick C.; Doerr, Hans W.; Cinatl, Jindrich

CORPORATE SOURCE: Institute of Medical Virology, Johann Wolfgang Goethe University Frankfurt, Frankfurt, 60596, Germany

SOURCE: Biochemical and Biophysical Research Communications (2005), 326(4), 905-908
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Initial in vitro investigations demonstrated type I interferons (IFNs: IFN-.alpha., IFN-.beta.) to inhibit replication of SARS coronavirus (SARS-CoV), but found the nucleoside analog ribavirin ineffective in Vero cells. In this report, ribavirin was shown to inhibit SARS-CoV replication in five different cell types of animal or human origin at therapeutically achievable concns. Since clin. anti-SARS-CoV activity of type I interferons or ribavirin is limited, we investigated the combination of IFN-.beta. and ribavirin. Detn. of the virus yield indicated highly synergistic anti-

SARS-CoV action of the combination suggesting the consideration of ribavirin plus IFN-.beta. for the treatment of SARS.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:930930 CAPLUS
DOCUMENT NUMBER: 141:343458
TITLE: Treatment of HMPV infections with ribavirin
INVENTOR(S): Maertzdorf, Jeroen; Simon, James Henry Matthew
PATENT ASSIGNEE(S): Vironovative B.V., Neth.
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1473037	A1	20041103	EP 2003-76299	20030502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
WO 2004096241	A1	20041111	WO 2004-NL293	20040503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-76299 A 20030502

AB The invention relates to antiviral agents and compns. comprising such agents to treat and/or prevent respiratory diseases, in particular those caused by human metapneumovirus. Provided is a method for treating or preventing respiratory tract infections in a subject infected with a mammalian MPV, said method comprising administering a nucleoside analog, preferably Ribavirin or a deriv. thereof, to said subject, and use of said nucleoside analog for the manuf. of a medicament for treating or preventing respiratory tract infections in a subject infected with a mammalian MPV.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:878414 CAPLUS
DOCUMENT NUMBER: 141:363038
TITLE: Sequences of SARS coronavirus and diagnostic and therapeutic use
INVENTOR(S): Haagmans, Bartholomeus Leonardus; Kuiken, Thijs; Fouchier, Ronaldus Adrianus Maria; Osterhaus, Albertus Dominicus Marcellinus Erasmus
PATENT ASSIGNEE(S): Vironovative B.V., Neth.
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089983	A2	20041021	WO 2004-NL229	20040408
WO 2004089983	A3	20050120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1466922	A1	20041013	EP 2003-76110	20030414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: EP 2003-76037 A 20030408
EP 2003-76110 A 20030414
EP 2003-77307 A 20030718

AB The invention relates to the field of virol. The invention provides an isolated essentially mammalian pos.-sense single stranded RNA virus (SARS) within the group of coronaviuses and components thereof.

L16 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:341396 CAPLUS
DOCUMENT NUMBER: 141:325198
TITLE: Inhibition of SARS coronavirus infection in vitro with clinically approved antiviral drugs
AUTHOR(S): Tan, Emily L. C.; Ooi, Eng Eong; Lin, Chin-Yo; Tan, Hwee Cheng; Ling, Ai Ee; Lim, Bing; Stanton, Lawrence W.
CORPORATE SOURCE: Genome Institute of Singapore, Singapore
SOURCE: Emerging Infectious Diseases (2004), 10(4), 581-586
CODEN: EIDIFA; ISSN: 1080-6040
PUBLISHER: National Center for Infectious Diseases, Centers for Disease Control and Prevention
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Severe acute respiratory syndrome (SARS) is an infectious disease caused by a newly identified human coronavirus (SARS-CoV). Currently, no effective drug exists to treat SARS-CoV infection. In this study, we investigated whether a panel of com. available antiviral drugs exhibit in vitro anti-SARS -CoV activity. A drug-screening assay that scores for virus-induced cytopathic effects on cultured cells was used. Tested were 19 clin. approved compds. from several major antiviral pharmacol. classes: nucleoside analogs, interferons, protease inhibitors, reverse transcriptase inhibitors, and neuraminidase inhibitors. Complete inhibition of cytopathic effects of SARS-CoV in culture was obsd. for interferon subtypes, .beta.-1b, .alpha.-n1, .alpha.-n3, and human leukocyte interferon a. These findings support clin. testing of approved interferons for the treatment of SARS.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L13 IBIB ABS 1-5

L13 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:108277 CAPLUS
TITLE: Dynamic changes of serum SARS coronavirus IgG, pulmonary function and radiography in patients recovering from SARS after hospital discharge
AUTHOR(S): Xie, Lixin; Liu, Youning; Fan, Baoxing; Xiao, Yueyong; Tian, Qing; Chen, Liangan; Zhao, Hong; Chen, Weijun
CORPORATE SOURCE: Dep. Respiratory Med., Chinese PLA General Hospital,

Beijing, 100853, Peop. Rep. China
SOURCE: Respiratory Research (2005), 6(1), No pp. given
CODEN: RREEBZ; ISSN: 1465-993X
URL: http://respiratory-research.com/content/pdf/1465-9921-6-5.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Objective: The intent of this study was to examine the recovery of individuals who had been hospitalized for severe acute respiratory syndrome (SARS) in the year following their discharge from the hospital. Parameters studied included serum levels of SARS coronavirus (SARS-CoV) IgG antibody, tests of lung function, and imaging data to evaluate changes in lung fibrosis. In addn., the authors explored the incidence of femoral head necrosis in some of the individuals recovering from SARS. Methods: The subjects of this study were 383 clin. diagnosed SARS patients in Beijing, China. They were tested regularly for serum levels of SARS-CoV IgG antibody and lung function and were given chest X-rays and/or high resoln. computerized tomog. (HRCT) examns. at the Chinese PLA General Hospital during the 12 mo that followed their release from the hospital. Those individuals who were found to have lung diffusion abnormality (transfer coeff. for carbon monoxide [DLO] < 80% of predicted value [pred]) received regular lung function tests and HRCT examns. in the follow-up phase to document the changes in their lung condition. Some patients who complained of joint pain were given magnetic resonance imaging (MRI) examns. of their femoral heads. Findings Of all the subjects, 81.2% (311 of 383 patients) tested pos. for serum SARS-CoV IgG. Of those testing pos., 27.3% (85 of 311 patients) were suffering from lung diffusion abnormality (DLCO < 80% pred) and 21.5% (67 of 311 patients) exhibited lung fibrotic changes. In the 12 mo duration of this study, all of the 40 patients with lung diffusion abnormities who were examd. exhibited some improvement of lung function and fibrosis detected by radiog. Of the individuals receiving MRI examns., 23.1% (18 of 78 patients) showed signs of femoral head necrosis. Interpretation The lack of sero-pos. SARS-CoV in some individuals suggests that there may have been some misdiagnosed cases among the subjects included in this study. Of those testing pos., the serum levels of SARS-CoV IgG antibody decreased significantly during the 12 mo after hospital discharge. Addnl., the authors found that the individuals who had lung fibrosis showed some spontaneous recovery. Finally, some of the subjects developed femoral head necrosis.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:930930 CAPLUS
DOCUMENT NUMBER: 141:343458
TITLE: Treatment of HMPV infections with ribavirin
INVENTOR(S): Maertzdorf, Jeroen; Simon, James Henry Matthew
PATENT ASSIGNEE(S): Vironovative B.V., Neth.
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1473037	A1	20041103	EP 2003-76299	20030502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
WO 2004096241	A1	20041111	WO 2004-NL293	20040503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-76299 A 20030502

AB The invention relates to antiviral agents and compns. comprising such agents to treat and/or prevent respiratory diseases, in particular those caused by human metapneumovirus. Provided is a method for treating or preventing respiratory tract infections in a subject infected with a mammalian MPV, said method comprising administering a nucleoside analog, preferably Ribavirin or a deriv. thereof, to said subject, and use of said nucleoside analog for the manuf. of a medicament for treating or preventing respiratory tract infections in a subject infected with a mammalian MPV.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:592228 CAPLUS

DOCUMENT NUMBER: 142:34357
TITLE: Coronavirus 3CL-pro proteinase cleavage sites: possible relevance to SARS virus pathology
AUTHOR(S): Kiemer, Lars; Lund, Ole; Brunak, Soren; Blom, Nikolaj
CORPORATE SOURCE: Center for Biological Sequence Analysis, BioCentrum-DTU, Technical University of Denmark, Lyngby, DK-2800, Den.
SOURCE: BMC Bioinformatics (2004), 5, No pp. given
CODEN: BBMIC4; ISSN: 1471-2105
URL: http://www.biomedcentral.com/content/pdf/1471-2105-5-72.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Despite the passing of more than a year since the first outbreak of Severe Acute Respiratory Syndrome (SARS), efficient counter-measures are still few and many believe that reappearance of SARS, or a similar disease caused by a coronavirus, is not unlikely. For other virus families like the picornaviruses it is known that pathol. is related to proteolytic cleavage of host proteins by viral proteinases. Furthermore, several studies indicate that virus proliferation can be arrested using specific proteinase inhibitors supporting the belief that proteinases are indeed important during infection. We set out to analyze and predict cleavage by the coronavirus main proteinase using computational methods. We retrieved sequence data on seven fully sequenced coronaviruses and identified the main 3CL proteinase cleavage sites in polyproteins using alignments. A neural network was trained to recognize the cleavage sites in the genomes obtaining a sensitivity of 87.0% and a specificity of 99,0%. Several proteins known to.be cleaved by other viruses were submitted to prediction as well. as proteins suspected relevant in coronavirus pathol. Cleavage sites were predicted in proteins such as the cystic fibrosis transmembrane conductance regulator (CFTR), transcription factors CREB-RP and OCT-1, and components of the ubiquitin pathway. Our prediction method NetCorona predicts coronavirus cleavage sites with high specificity and several potential cleavage candidates were identified which might be important to elucidate coronavirus pathol. Furthermore, the method might assist in design of proteinase inhibitors for treatment of SARS and possible future diseases caused by coronaviruses.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:566640 CAPLUS
DOCUMENT NUMBER: 141:105262
TITLE: Human monoclonal antibodies against human interleukin 8 for diagnosis and treatment of immune, autoimmune, inflammatory, infectious and neoplastic disorders
INVENTOR(S): Teeling, Jessica; Parren, Paul; Bàadsgaard, Ole D. M. Sc.; Hudson, Debra; Petersen, Jorgen
PATENT ASSIGNEE(S): Medarex, Inc., USA; Genmab A/S
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058797	A2	20040715	WO 2003-US40039	20031216
US 2004208873	A1	20041021	US 2003-738120	20031216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-433728P P 20021216

AB Isolated human monoclonal antibodies which bind to IL-8 (e.g., human IL-8) are disclosed. The human antibodies can be produced in a hybridoma, transfectoma or in a non-human transgenic animal, e.g., a transgenic mouse, capable of producing multiple isotypes of human monoclonal antibodies by undergoing V-D-J recombination and isotype switching. Also disclosed are pharmaceutical compns. comprising the human antibodies, non-human transgenic animals, hybridomas, and transfectomas which produce the human antibodies, and therapeutic and diagnostic methods for using the human antibodies.

L13 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:80343 CAPLUS
DOCUMENT NUMBER: 140:122836
TITLE: Use of 2,3-alkylcarbonyloxybenzoic acids, derivatives and analogues therefrom in the treatment of tissue and cellular dysfunction, damage and injury in mammals

INVENTOR(S): Stec, Karen; Rubinstein, Israel; Eiznhamer, David; Xu, Ze-qu; Flavin, Michael
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004019022	A1	20040129	US 2003-622302	20030718
WO 2004010989	A1	20040205	WO 2003-US23644	20030718

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-398523P P 20020725

AB A method for the treatment of cellular and tissue damage is disclosed. The inventive method comprises the use of 2,3-alkylcarbonyloxybenzoic acid and salts thereof for the prevention and treatment of dysfunction, damage, and/or injuries to organs, tissues and/or cells in human or animal subjects caused by diseases, infections and conditions such as pneumonia, coronavirus, multiple transfusions, trauma, ischemic-reperfusion dysfunctions, stroke, drug overdose, and severe acute respiratory syndrome. The 2,3-alkylcarbonyloxybenzoic acid may be used alone or in combination with other therapeutic agents such as antibiotics. The acid may be administered in any practical delivery form, and in free acid or buffered form.

=> D L15 IBIB ABS 1-15

L15 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:238669 CAPLUS
DOCUMENT NUMBER: 142:291330
TITLE: Targeted delivery of antiviral compounds through hemoglobin bioconjugates
INVENTOR(S): Adamson, J. Gordon; Bell, David; Ng, Nancy; Biessels,

Pieter
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 32 pp., Cont.-in-part of U.S. Ser. No. 231,062.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005059576	A1	20050317	US 2004-846597	20040517
CA 2236344	AA	19991030	CA 1998-2236344	19980430
US 6479637	B1	20021112	US 1999-302351	19990430
US 2003013642	A1	20030116	US 2002-231062	20020830

PRIORITY APPLN. INFO.: CA 1998-2236344 A 19980430
US 1999-302351 A1 19990430
US 2002-231062 A2 20020830
US 2003-470445P P 20030515
US 2003-513575P P 20031024

AB This invention relates to targeted delivery of anti-viral compds. through protein bioconjugation. More particularly, it relates to an anti-viral compd. conjugated to a protein, such as Hb and to a method of treating a viral infection using said conjugate. The invention also provides a method of targeted drug delivery of an anti-viral nucleoside analog to macrophages, cells comprising a Hb receptor and to CD163 bearing cells.

L15 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:216597 CAPLUS
DOCUMENT NUMBER: 142:291323
TITLE: Compositions and methods for the treatment of severe acute respiratory syndrome (SARS)
INVENTOR(S): Hardee, Greg; Dellamary, Luis
PATENT ASSIGNEE(S): Isis Phramaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 217 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020885	A2	20050310	WO 2004-US16196	20040521

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2003-472774P P 20030521
AB The invention provides compns. and methods for treating a coronavirus infection, esp. a SARS CoV infection. The compns. comprise an antiviral nucleoside or mimetic thereof, or an antiviral antisense agent, in a form suitable for pulmonary or nasal delivery. The methods comprise administration to a patient in need thereof the effective amt. of an antiviral compn. by pulmonary or nasal instillation.

L15 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1127477 CAPLUS
DOCUMENT NUMBER: 142:69880
TITLE: Methods for identification of coronaviruses by PCR amplification of a RdRp orf-1b or nsp11 target region for diagnostic application
INVENTOR(S): Ecker, David J.; Hofstadler, Steven A.; Sampath, Rangarajan; Blyn, Lawrence B.; Hall, Thomas A.; Massire, Christian
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111187	A2	20041223	WO 2004-US12671	20040423

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-466009P P 20030426
US 2003-467768P P 20030502
US 2003-468743P P 20030507
US 2004-542510P P 20040206

AB The present invention provides a method for rapid identification and quantitation of coronavirus by amplification of a segment of coronavirus nucleic acid followed by anal. by mass spectrometry. The compns. provide for characterization of the mol. masses and base compns. of coronavirus nucleic acids which are used to rapidly identify coronavirus.

L15 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1127101 CAPLUS
DOCUMENT NUMBER: 142:49201
TITLE: Inhibiting Coronaviridae viral replication and treating Coronaviridae viral infection with nucleoside compounds
INVENTOR(S): Olsen, David B.; Tomassini, Joanne E.; Mao, Shi-Shan; Carroll, Steven S.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp., which
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004259934	A1	20041223	US 2004-832945	20040427

PRIORITY APPLN. INFO.: US 2003-467068P P 20030501
US 2003-470658P P 20030515
OTHER SOURCE(S): MARPAT 142:49201

AB Infection by a Coronaviridae virus (e.g. a coronavirus) and/or illness due to a Coronaviridae virus are treated or protected against by administration of a therapeutically or prophylactically effective amt. of certain nucleoside compds. and derivs. thereof, either alone or in a compn. comprising the nucleoside compd. or its deriv. and a pharmaceutically acceptable carrier. In addn., replication of a Coronaviridae virus is inhibited by administration of the nucleoside compds. and derivs. thereof, either alone or in

pharmaceutical compns. The nucleosides are particularly suitable for use in treating or prophylaxis of an infection by the SARS virus and/or in treating or prophylaxis of SARS, and for use in inhibiting replication of the SARS virus. The nucleoside compds. and derivs. can optionally be administered in combination with other agents active against the Coronaviridae virus and/or an illness due to the virus. The nucleoside compds. are also for use in the manuf. of medicaments for the inhibition of Coronaviridae virus replication, for the treatment or prophylaxis of Coronaviridae virus infection, and/or for the treatment or prophylaxis of an illness due to a Coronaviridae virus (e.g., the SARS virus). In addn., the compds. are for use as medicaments for the inhibition of Coronaviridae virus replication, for the treatment or prophylaxis of Coronaviridae virus infection, and/or for the treatment or prophylaxis of an illness due to a Coronaviridae virus. Compds. of the invention include e.g. 4-Amino-7-(2-C-methyl-.beta.-D-ribofuranosyl)-7H-pyrrolo[2,3-d]pyrimidine (prepn. described).

L15 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1124599 CAPLUS
DOCUMENT NUMBER: 142:49199
TITLE: Compositions and methods for treating coronavirus infection and SARS with interferons
INVENTOR(S): Blatt, Lawrence M.
PATENT ASSIGNEE(S): Intermune, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110392	A2	20041223	WO 2004-US7819	20040312

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,

TD, TG
US 2005002901 A1 20050106 US 2004-814701 20040330
PRIORITY APPLN. INFO.: US 2003-459783P P 20030401
AB The present invention provides methods of treating a coronavirus infection, and methods of reducing viral load, or reducing the time to viral clearance, or reducing morbidity or mortality in the clin. outcomes, in patients suffering from a coronavirus infection. The present invention further provides methods of reducing the risk that an individual will develop a pathol. coronavirus infection, that has clin. sequelae. The present invention further provides methods of reducing the risk that an individual will develop SARS. The present invention further provides methods of treating SARS. The methods generally involve administering a therapeutically effective amt. of a Type I or Type III interferon receptor agonist and/or a Type II interferon receptor agonist for the treatment of a coronavirus infection.

L15 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1087826 CAPLUS
DOCUMENT NUMBER: 142:92001
TITLE: Ribavirin and interferon-.beta. synergistically inhibit SARS-associated coronavirus replication in animal and human cell lines
AUTHOR(S): Morgenstern, Birgit; Michaelis, Martin; Baer, Patrick C.; Doerr, Hans W.; Cinatl, Jindrich
CORPORATE SOURCE: Institute of Medical Virology, Johann Wolfgang Goethe University Frankfurt, Frankfurt, 60596, Germany
SOURCE: Biochemical and Biophysical Research Communications (2005), 326(4), 905-908
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Initial in vitro investigations demonstrated type I interferons (IFNs: IFN-.alpha., IFN-.beta.) to inhibit replication of SARS coronavirus (SARS-CoV), but found the nucleoside analog ribavirin ineffective in Vero cells. In this report, ribavirin was shown to inhibit SARS-CoV replication in five different cell types of animal or human origin at therapeutically achievable concns. Since clin. anti-SARS-CoV activity of type I interferons or ribavirin is limited, we investigated the combination of IFN-.beta. and ribavirin. Detn. of the virus yield indicated highly synergistic anti-SARS-CoV action of the combination suggesting the consideration of ribavirin plus IFN-.beta. for the treatment of SARS.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:930930 CAPLUS
DOCUMENT NUMBER: 141:343458
TITLE: Treatment of HMPV infections with ribavirin
INVENTOR(S): Maertzdorf, Jeroen; Simon, James Henry Matthew
PATENT ASSIGNEE(S): Vironovative B.V., Neth.
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1473037	A1	20041103	EP 2003-76299	20030502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
WO 2004096241	A1	20041111	WO 2004-NL293	20040503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-76299 A 20030502

AB The invention relates to antiviral agents and compns. comprising such agents to treat and/or prevent respiratory diseases, in particular those caused by human metapneumovirus. Provided is a method for treating or preventing respiratory tract infections in a subject infected with a mammalian MPV, said method comprising administering a nucleoside analog, preferably Ribavirin or a deriv. thereof, to said subject, and use of said nucleoside analog for the manuf. of a medicament for treating or preventing respiratory tract infections in a subject infected with a mammalian MPV.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:878414 CAPLUS
DOCUMENT NUMBER: 141:363038
TITLE: Sequences of SARS coronavirus and diagnostic and therapeutic use
INVENTOR(S): Haagmans, Bartholomeus Leonardus; Kuiken, Thijs; Fouchier, Ronaldus Adrianus Maria; Osterhaus, Albertus Dominicus Marcellinus Erasmus
PATENT ASSIGNEE(S): Vironovative B.V., Neth.
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089983	A2	20041021	WO 2004-NL229	20040408
WO 2004089983	A3	20050120		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1466922	A1	20041013	EP 2003-76110	20030414

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: EP 2003-76037 A 20030408
EP 2003-76110 A 20030414
EP 2003-77307 A 20030718

AB The invention relates to the field of virol. The invention provides an isolated essentially mammalian pos.-sense single stranded RNA virus (SARS) within the group of coronaviuses and components thereof.

L15 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:789787 CAPLUS
DOCUMENT NUMBER: 142:32433
TITLE: Application of real-time PCR for testing antiviral compounds against Lassa virus, SARS

coronavirus and Ebola virus in vitro
AUTHOR(S): Gunther, Stephan; Asper, Marcel; Roser, Christina; Luna, Luciano K. S.; Drosten, Christian; Becker-Ziaja, Beate; Borowski, Peter; Chen, Huan-Ming; Hosmane, Ramachandra S.
CORPORATE SOURCE: Department of Virology, Bernhard-Nocht-Institute of Tropical Medicine, Hamburg, D-20359, Germany
SOURCE: Antiviral Research (2004), 63(3), 209-215
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This report describes the application of real-time PCR for testing antivirals against highly pathogenic viruses such as Lassa virus, SARS coronavirus and Ebola virus. The test combines classical cell culture with a quant. real-time PCR read-out. The assay for Lassa virus was validated with ribavirin, which showed an IC50 of 9 .mu.g/mL. Small-scale screening identified a class of imidazole nucleoside/nucleotide analogs with antiviral activity against Lassa virus. The analogs contained either dinitrile or diester groups at the imidazole 4,5-positions, and many of which possessed an acyclic sugar or sugar phosphonate moiety at the imidazole 1-position. The IC50 values of the most active compds. ranged from 5 to 21 .mu.g/mL. The compds. also inhibited replication of SARS coronavirus and Ebola virus in analogous assays, although to a lesser extent than Lassa virus.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:751456 CAPLUS
DOCUMENT NUMBER: 142:150677
TITLE: Human SARS-coronavirus RNA-dependent RNA polymerase: Activity determinants and nucleoside analogue inhibitors
AUTHOR(S): Azzi, Arezki; Lin, Sheng-Xiang
CORPORATE SOURCE: Molecular Endocrinology and Oncology Research Center, Laval University Medical Center (CHUL), Quebec City, QC, Can.
SOURCE: Proteins: Structure, Function, and Bioinformatics (2004), 57(1), 12-14
CODEN: PSFBAF
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A homol. model of the SARS polymerase is built using the 3D jury

system. The capability of the 3D-jury in using consensus between Meta prediction methods makes it a very reliable tool for model building. As the sequence alignment search for SARS RNA-dependent RNA polymerase (RdRp) conducted with BLAST did not yield a homologous structure, the 3D jury Meta predictor is used to identify a homol. model. The RdRp function was assigned to a C-terminal segment of 537 residues out of the nsP12 932 residues with a highly significant score. The power of this method is illustrated by the fact that even with less than 10% sequence identity, the Rabbit Hemorrhagic Disease Virus (RHDV) RdR polymerase, was identified as a homologous structure, based on a combination of motif search, fold recognition, and structure-based alignment orchestrated by the 3D-jury Meta server. The present RdRp 3D-model highlighted by the domain structure and by the active site architecture can provide a rationale for the design of inhibitors for the synthesis of viral RNA.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:454317 CAPLUS

DOCUMENT NUMBER: 141:220713

TITLE: Multiple enzymatic activities associated with Severe acute respiratory syndrome coronavirus helicase

AUTHOR(S): Ivanov, Konstantin A.; Thiel, Volker; Dobbe, Jessika C.; Van Der Meer, Yvonne; Snijder, Eric J.; Ziebuhr, John

CORPORATE SOURCE: Institute of Virology and Immunology, University of Wuerzburg, Wuerzburg, Germany

SOURCE: Journal of Virology (2004), 78(11), 5619-5632
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Severe acute respiratory syndrome coronavirus (SARS -CoV), a newly identified group 2 coronavirus, is the causative agent of severe acute respiratory syndrome, a life-threatening form of pneumonia in humans. Coronavirus replication and transcription are highly specialized processes of cytoplasmic RNA synthesis that localize to virus-induced membrane structures and were recently proposed to involve a complex enzymic machinery that, besides RNA-dependent RNA polymerase, helicase, and protease activities, also involves a series of RNA-processing enzymes that are not found in most other RNA virus families. Here, we characterized the enzymic activities of a recombinant form of the SARS-CoV helicase (nonstructural protein [nsp] 13),

a superfamily 1 helicase with an N-terminal zinc-binding domain. We report that nsp13 has both RNA and DNA duplex-unwinding activities. SARS-CoV nsp13 unwinds its substrates in a 5'-to-3' direction and features a remarkable processivity, allowing efficient strand sepn. of extended regions of double-stranded RNA and DNA. Characterization of the nsp13-assocd. (deoxy)nucleoside triphosphatase ((d)NTPase) activities revealed that all natural nucleotides and deoxynucleotides are substrates of nsp13, with ATP, dATP, and GTP being hydrolyzed slightly more efficiently than other nucleotides. Furthermore, we established an RNA 5'-triphosphatase activity for the SARS-CoV nsp13 helicase which may be involved in the formation of the 5' cap structure of viral RNAs. The data suggest that the (d)NTPase and RNA 5'-triphosphatase activities of nsp13 have a common active site. Finally, we established that, in SARS-CoV-infected Vero E6 cells, nsp13 localizes to membranes that appear to be derived from the endoplasmic reticulum and are the likely site of SARS-CoV RNA synthesis.

REFERENCE COUNT: 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:416110 CAPLUS

DOCUMENT NUMBER: 141:199516

TITLE: Inhibition of severe acute respiratory syndrome-associated coronavirus (SARSCoV) by calpain inhibitors and .beta.-D-N4-hydroxycytidine

AUTHOR(S): Barnard, Dale L.; Hubbard, Valerie D.; Burton, Jared; Smee, Donald F.; Morrey, John D.; Otto, Michael J.; Sidwell, Robert W.

CORPORATE SOURCE: Institute for Antiviral Research, Utah State University, Logan, UT, USA

SOURCE: Antiviral Chemistry & Chemotherapy (2004), 15(1), 15-22
CODEN: ACCHEH; ISSN: 0956-3202

PUBLISHER: International Medical Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We evaluated two types of compds. for efficacy in inhibiting SARSCoV replication in vitro: calpain inhibitors (a class of cellular cysteine proteinases) and a no. of nucleoside analogs. Cytopathic effect redn. assays visually detd. with spectrophotometric verification by neutral red (NR) uptake assay were used to evaluate cytotoxicity and antiviral potency of the compds. Significantly inhibitory compds. were then evaluated in virus yield redn. assays. Two calpain inhibitors, Val-Leu-CHO (calpain inhibitor VI) and Z-Val-Phe-Ala-CHO (calpain inhibitor III), were the most potent inhibitors of SARSCoV. By virus

yield redn. assay, calpain inhibitor VI had a 90% effective concn. (EC90) of 3 .mu.M and calpain inhibitor III had an EC90 of 15 .mu.M. .beta.-D-N4-hydroxycytidine was the most selective nucleoside analog inhibitor with an EC90 of 6 .mu.M by virus yield redn. assay. These compds. or analogs warrant further evaluation as potential therapies for treating SARS or could be used as lead compds. for discovery of more potent SARS CoV inhibitors.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:341396 CAPLUS

DOCUMENT NUMBER: 141:325198

TITLE: Inhibition of SARS coronavirus infection in vitro with clinically approved antiviral drugs

AUTHOR(S): Tan, Emily L. C.; Ooi, Eng Eong; Lin, Chin-Yo; Tan, Hwee Cheng; Ling, Ai Ee; Lim, Bing; Stanton, Lawrence W.

CORPORATE SOURCE: Genome Institute of Singapore, Singapore

SOURCE: Emerging Infectious Diseases (2004), 10(4), 581-586 CODEN: EIDIFA; ISSN: 1080-6040

PUBLISHER: National Center for Infectious Diseases, Centers for Disease Control and Prevention

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Severe acute respiratory syndrome (SARS) is an infectious disease caused by a newly identified human coronavirus (SARS-CoV). Currently, no effective drug exists to treat SARS-CoV infection. In this study, we investigated whether a panel of com. available antiviral drugs exhibit in vitro anti-SARS -CoV activity. A drug-screening assay that scores for virus-induced cytopathic effects on cultured cells was used. Tested were 19 clin. approved compds. from several major antiviral pharmacol. classes: nucleoside analogs, interferons, protease inhibitors, reverse transcriptase inhibitors, and neuraminidase inhibitors. Complete inhibition of cytopathic effects of SARS-CoV in culture was obsd. for interferon subtypes, .beta.-1b, .alpha.-n1, .alpha.-n3, and human leukocyte interferon a. These findings support clin. testing of approved interferons for the treatment of SARS.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:80343 CAPLUS
DOCUMENT NUMBER: 140:122836
TITLE: Use of 2,3-alkylcarbonyloxybenzoic acids, derivatives and analogues therefrom in the treatment of tissue and cellular dysfunction, damage and injury in mammals
INVENTOR(S): Stec, Karen; Rubinstein, Israel; Eiznhamer, David; Xu, Ze-qu; Flavin, Michael
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004019022	A1	20040129	US 2003-622302	20030718
WO 2004010989	A1	20040205	WO 2003-US23644	20030718

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-398523P P 20020725
AB A method for the treatment of cellular and tissue damage is disclosed. The inventive method comprises the use of 2,3-alkylcarbonyloxybenzoic acid and salts thereof for the prevention and treatment of dysfunction, damage, and/or injuries to organs, tissues and/or cells in human or animal subjects caused by diseases, infections and conditions such as pneumonia, coronavirus, multiple transfusions, trauma, ischemic-reperfusion dysfunctions, stroke, drug overdose, and severe acute respiratory syndrome. The 2,3-alkylcarbonyloxybenzoic acid may be used alone or in combination with other therapeutic agents such as antibiotics. The acid may be administered in any practical delivery form, and in free acid or buffered form.

L15 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:960198 CAPLUS
DOCUMENT NUMBER: 140:141632
TITLE: Molecular model of SARS coronavirus

polymerase: implications for biochemical functions and drug design

AUTHOR(S): Xu, Xiang; Liu, Yunqing; Weiss, Susan; Arnold, Eddy; Sarafianos, Stefan G.; Ding, Jianping

CORPORATE SOURCE: Shanghai Institutes for Biological Sciences, Institute of Biochemistry and Cell Biology, Key Laboratory of Proteomics, Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China

SOURCE: Nucleic Acids Research (2003), 31(24), 7117-7130
CODEN: NARHAD; ISSN: 0305-1048

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The causative agent of severe acute respiratory syndrome (SARS) is a previously unidentified coronavirus, SARS-CoV. The RNA-dependent RNA polymerase (RdRp) of SARS-CoV plays a pivotal role in viral replication and is a potential target for anti-SARS therapy. There is a lack of structural or biochem. data on any coronavirus polymerase. To provide insights into the structure and function of SARS-CoV RdRp, we have located its conserved motifs that are shared by all RdRps, and built a three-dimensional model of the catalytic domain. The structural model permits us to discuss the potential functional roles of the conserved motifs and residues in replication and their potential interactions with inhibitors of related enzymes. We predict the following important structural attributes for potential anti-SARS-CoV RdRp nucleotide analog inhibitors: hydrogen-bonding capability for the 2' and 3' groups of the sugar ring and C3' endo sugar puckering, and the absence of a hydrophobic binding pocket for non-nucleoside analog inhibitors similar to those obsd. in hepatitis C virus RdRp and human immunodeficiency virus type 1 reverse transcriptase. We propose that the clin. obsd. resistance of SARS to ribavirin is probably due to perturbation of the conserved motif A that controls rNTP binding and fidelity of polymn. Our results suggest that designing anti-SARS therapies can benefit from successful experiences in design of other antiviral drugs. This work should also provide guidance for future biochem. expts.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> "fibrosis" (l) L1
28868 "FIBROSIS"
L18 43 "FIBROSIS" (L) L1

=> pirfenidone and L18
114 PIRFENIDONE
L19 0 PIRFENIDONE AND L18

=> treatment and l18
2006213 TREATMENT
185728 TREATMENTS
2105955 TREATMENT
(TREATMENT OR TREATMENTS)
L20 43 TREATMENT AND L18

=> interferon and l18
65244 INTERFERON
67532 INTERFERONS
82016 INTERFERON
(INTERFERON OR INTERFERONS)
L21 20 INTERFERON AND L18

=> nucleoside and L18
43410 NUCLEOSIDE
29795 NUCLEOSIDES
54411 NUCLEOSIDE
(NUCLEOSIDE OR NUCLEOSIDES)
L22 8 NUCLEOSIDE AND L18

=> D L22 IBIB ABS 1-8

L22 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:69095 CAPLUS
TITLE: Extended lamivudine treatment in patients with HBeAg-negative chronic hepatitis B
AUTHOR(S): Rizzetto, Mario; Tassopoulos, Nicholas C.; Goldin, Robert D.; Esteban, Rafael; Santantonio, Teresa; Heathcote, E. Jenny; Lagget, Marco; Taak, Namrata K.; Woessner, Mary A.; Gardner, Stephen D.
CORPORATE SOURCE: Experimental Department of Gastroenterology, San Giovanni Battista Hospital C.So Bramante, Turin, 88 10126, Italy
SOURCE: Journal of Hepatology (2005), 42(2), 173-179
CODEN: JOHEEC; ISSN: 0168-8278
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background/Aims: The histol. and clin. outcome of lamivudine 100 mg/day was assessed in 76 HBeAg-neg. chronic hepatitis B patients previously randomised to a double-blind comparison study of lamivudine and placebo.

Methods: Paired liver biopsies were available before 1 yr of randomised lamivudine treatment and after 2 years of further open-label treatment for 48 patients. Serum samples were analyzed for hepatitis B markers and ALT levels (n=74). Results: The histol. activity index improved, remained unchanged and worsened in 64, 32 and 5%, resp., for patients without YMDD-variant HBV compared to 15, 54 and 31% with the variant. None of the 42/48 patients without cirrhosis at baseline progressed to cirrhosis. Of 24/48 patients without bridging fibrosis at pre-treatment, 83% (20/24) did not progress to bridging fibrosis. Median HBV DNA remained below the lower limit of detection and ALT .ltoreq.1 times the ULN for patients without the variant whereas levels gradually increased to 11.3 Meq/mL (bDNA assay) and 2 times the upper limit of normal by month 24 for patients with variant. Conclusions: The clin. benefit of lamivudine is greatest for patients without YMDD variants over 2 years of extended treatment. Addnl. therapies should be considered for patients with YMDD variants.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:126760 CAPLUS
DOCUMENT NUMBER: 139:270294
TITLE: Lamivudine therapy in renal allograft recipients with hepatitis B virus infection
AUTHOR(S): Tsang, W. K.; Tong, K. L.; Chan, H. W. H.
CORPORATE SOURCE: Department of Medicine and Geriatrics, Division of Nephrology, Princess Margaret Hospital, Hong Kong, Peop. Rep. China
SOURCE: Transplantation Proceedings (2003), 35(1), 278-279
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Renal allograft recipients, due to heavy immunosuppression, are at risk of developing more aggressive hepatitis, cirrhosis, and, less frequently, hepatocellular carcinoma resulting in higher liver-related morbidity and mortality rates. Interferon .alpha. has been reported to be assocd. with high incidence of acute rejection in renal transplant patients. Lamivudine is a new cytidine nucleoside analog that inhibits DNA synthesis through interference with the reverse transcriptase activity of hepatitis B virus (HBV). It has been shown to be effective in suppressing HBV replication in immunocompetent patients with HBV infection. Preliminary studies show that lamivudine is useful in treating chronic hepatitis B in renal transplant patients. We studied

the efficacy and safety of lamivudine in Asian renal allograft recipients with HBV infection. Lamivudine was found to be safe and very effective in the suppression of HBV replication, normalization of alanine aminotransferase (ALT), enhancement of HBeAg seroconversion, and seldomly, eradication of HBV. It can be a useful therapeutic option for HBV infection in renal transplant recipients with abnormal ALT. Effects of long-term treatment and/or combination antiviral therapy on viral replication, fibrosis, and hepatocellular carcinoma incidence should be evaluated.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:432626 CAPLUS
DOCUMENT NUMBER: 133:37500
TITLE: Liver disease-significant improvement with lamivudine
AUTHOR(S): Leung, Nancy
CORPORATE SOURCE: Department of Medicine and Therapeutics, Prince of Wales Hospital, Shatin, Hong Kong
SOURCE: Journal of Medical Virology (2000), 61(3), 380-385
CODEN: JMVIDB; ISSN: 0146-6615
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 20 refs. The natural history of chronic hepatitis B virus (HBV) infection is highly variable, ranging from a benign course to one of shortened life expectancy. Liver histol. represents an accurate tool for assessing progressive liver disease, and has been used in five recent Phase III clin. trials of the oral nucleoside analog, lamivudine, 100 mg/day, in patients with chronic hepatitis B. Significant improvements in the Knodell histol. activity index (HAI) score were reported with lamivudine, with greater decreases noted after 2 yr of therapy, consistent with continued alanine transaminase (ALT) normalization. Histol. data showed that lamivudine therapy can resolve or lessen the progression of fibrosis, and reduce the progression to cirrhosis in patients with chronic hepatitis B. These trials also showed that lamivudine provoked significant enhancement of hepatitis B e antigen (HBeAg) seroconversion compared with placebo, and had a profound effect on serum HBV DNA, resulting in rapid suppression of viremia. The emergence of variants with a mutation in the YMDD (tyrosine-methionine-aspartate-aspartate) motif did not cause significant worsening of the Knodell HAI score. In conclusion, lamivudine is the first oral antiviral therapy for the treatment of chronic hepatitis B. It reduces significantly the severity of liver disease and

reduces progression to cirrhosis. In addn., because lamivudine is well tolerated it represents a viable therapeutic option that may improve the prognosis of patients with chronic hepatitis B.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:14316 CAPLUS

DOCUMENT NUMBER: 132:44564

TITLE: Famciclovir treatment of chronic hepatitis B in heart transplant recipients: a prospective trial

AUTHOR(S): Wedemeyer, Heiner; Boker, Klaus H. W.; Pethig, Klaus; Petzold, Dieter R.; Flemming, Peer; Tillmann, Hans Ludger; Vollmar, Jens; Basturk, Murat; Goldmann, Ekaterina; Griffin, Karen E.; Haverich, Axel; Manns, Michael Peter

CORPORATE SOURCE: Departments of Gastroenterology, Cardiovascular Surgery, Virology, and Pathology, Medizinische Hochschule Hannover, Hannover, D-30625, Germany

SOURCE: Transplantation (1999), 68(10), 1503-1511
CODEN: TRPLAU; ISSN: 0041-1337

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hepatitis B may take a rapid and aggressive course in patients under immunosuppression. Nucleoside analogs have been shown to suppress viral replication effectively. To investigate the effect of famciclovir in immunosuppressed patients, 21 heart transplant recipients with chronic hepatitis B infection were included in a prospective study. Patients have been treated with Famciclovir for a median of 14 mo. Hepatitis B virus replication and biochem. parameters were regularly tested and liver biopsies were taken before treatment and after a median time of 7 mo. HBV-polymerase was sequenced in all patients before therapy and in those patients who experienced virol. breakthrough. Nineteen patients were treated for at least 6 mo. Hepatitis B virus-DNA levels declined in all patients and became neg. in 8 patients. Mean hepatitis B virus-DNA levels decreased from 199.+-.269 to 34.+-.53 pg/mL after 24 wk (P=0.003). During treatment HBeAg became neg. in five patients. Mean alanine aminotransferase decreased from 42.+-.26 to 24.+-.10 U/L (P=0.006). Histol. anal. revealed improved inflammatory activity according to the Ishak-score in 11/16 (69%) patients. Total inflammatory activity scores decreased from 8 to 6 (median, NS), but interface hepatitis score (P=0.02) and lobular inflammation score (P=0.006) improved significantly. Median fibrosis scores fell from 5 to 3 (P=0.002). Three patients

developed virol. breakthrough on famciclovir after 7, 8, and 26 mo of treatment showing HBV-polymerase amino acid changes L528 M, S567A, and I581K, resp. Famciclovir improves not only biochem. and virol. features but also hepatic inflammation and liver fibrosis in patients with chronic hepatitis B under heavy immunosuppression. Virol. breakthrough may develop and requires close monitoring.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:724911 CAPLUS

DOCUMENT NUMBER: 131:317377

TITLE: Lamivudine as initial treatment for chronic hepatitis B in the United States

AUTHOR(S): Dienstag, Jules L.; Schiff, Eugene R.; Wright, Teresa L.; Perrillo, Robert P.; Hann, Hie-Won L.; Goodman, Zachary; Crowther, Lynn; Condreay, Lynn D.; Woessner, Mary; Rubin, Marc; Brown, Nathaniel A.; Bacon, B. R.; Baker, A.; Caldwell, S. H.; Casey, D. E., Jr.; Davis, G. L.; Everson, G. T.; Foust, R. T.; Gish, R.; Gitlin, N.; Gordon, S. C.; Grimm, L. S.; Jacobson, I.; Kowdley, K. V.; Lee, W. M.; Lewis, J. H.; Lindsay, K.; Marsano, L.; O'Brien, C. B.; Rakela, J.; Riely, C.; Rustgi, V. K.; Sanchez Rodriguez, C. I.; Sceff, L.; Shiffman, M. L.; Tamburro, C. H.; Tong, M. J.

CORPORATE SOURCE: U. S. Lamivudine Investigator Group, Gastrointestinal Unit (Medical Services) and Liver-Biliary-Pancreas Center, Massachusetts General Hospital, Boston, MA, 02114, USA

SOURCE: New England Journal of Medicine (1999), 341(17), 1256-1263
CODEN: NEJMAG; ISSN: 0028-4793

PUBLISHER: Massachusetts Medical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Although the nucleoside analog lamivudine has shown promise in patients with chronic hepatitis B, long-term data on patients from the United States are lacking. We randomly assigned previously untreated patients with chronic hepatitis B to receive either 100 mg of oral lamivudine or placebo daily for 52 wk. We then followed them for an addnl. 16 wk to evaluate post-treatment safety and the durability of responses. The primary end point with respect to efficacy was a redn. of at least 2 points in the score on the Histol. Activity Index. On this scale, scores can range from 0 (normal) to 22 (most severe abnormalities). Of the 143 randomized patients, 137 were included in the

efficacy anal.: 66 in the lamivudine group and 71 in the placebo group. The other six patients were excluded at the base-line visit because of the absence of a documented history of hepatitis B surface antigen for at least six months. After 52 wk of treatment, lamivudine recipients were more likely than placebo recipients to have a histol. response (52 percent vs. 23 percent, P<0.001), loss of hepatitis B e antigen (HBeAg) in serum (32 percent vs. 11 percent, P=0.003), sustained suppression of serum hepatitis B virus (HBV) DNA to undetectable levels (44 percent vs. 16 percent, P<0.001), and sustained normalization of serum alanine aminotransferase levels (41 percent vs. 7 percent, P<0.001), and they were less likely to have increased hepatic fibrosis (5 percent vs. 20 percent, P=0.01). Lamivudine recipients were also more likely to undergo HBeAg seroconversion, defined as the loss of HBeAg, undetectable levels of serum HBV DNA, and the appearance of antibodies against HBeAg (17 percent vs. 6 percent, P=0.04). HBeAg responses persisted in most patients for 16 wk after the discontinuation of treatment. Lamivudine was well tolerated. Self-limited post-treatment elevations in serum alanine aminotransferase were more common in lamivudine recipients: 25 percent had serum alanine aminotransferase levels that were at least three times base-line levels, as compared with 8 percent of placebo recipients (P=0.01). The clin. condition of all patients remained stable during the study. In U.S. patients with previously untreated chronic hepatitis B, one year of lamivudine therapy had favorable effects on histol., virol., and biochem. features of the disease and was well tolerated. HBeAg responses were usually sustained after treatment.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:522024 CAPLUS
DOCUMENT NUMBER: 131:165011
TITLE: Lamivudine for chronic delta hepatitis
AUTHOR(S): Lau, Daryl T.-Y.; Doo, Edward; Park, Yoon; Kleiner, David E.; Schmid, Peter; Kuhns, Mary C.; Hoofnagle, Jay H.
CORPORATE SOURCE: Liver Diseases Section, Digestive Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, Abbott Park, IL, USA
SOURCE: Hepatology (Philadelphia) (1999), 30(2), 546-549
CODEN: HPTLD9; ISSN: 0270-9139
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chronic delta hepatitis is a severe form of chronic liver disease caused

by hepatitis delta virus (HDV) infection superimposed on chronic hepatitis B or the hepatitis B surface antigen (HBsAg) carrier state. Therapy of delta hepatitis is currently unsatisfactory. We have evaluated lamivudine (3-thiacytidine), an oral nucleoside analog with marked effects against hepatitis B, as therapy in 5 patients with chronic hepatitis D. Five men, ages 38 to 65 yr, were treated. All had HBsAg, antibody to HDV, and HDV RNA in serum, as well as persistent elevations in alanine aminotransferase (ALT) levels and liver histol. showing severe chronic hepatitis with fibrosis or cirrhosis. Lamivudine was given in a dose of 100 mg orally daily for 12 mo. Patients were monitored carefully and tested for HBsAg, HBV-DNA and HDV-RNA levels serially during the year of treatment and for 6 mo thereafter. Liver biopsies were performed before therapy and repeated after 1 yr. Serum levels of HBV DNA fell rapidly in all 5 patients, becoming undetectable even by polymerase chain reaction (PCR) in 4. However, all 5 patients remained HBsAg- and HDV-RNA-pos., and serum ALT levels and liver histol. did not improve. All patients tolerated therapy well. When lamivudine was stopped, HBV-DNA levels returned to pretreatment values without a change in disease activity. Lamivudine is a potent inhibitor of HBV-DNA replication, but does not improve disease activity or lower HDV-RNA levels in patients with chronic delta hepatitis.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:576865 CAPLUS
DOCUMENT NUMBER: 129:159923
TITLE: Therapy of viral hepatitis
AUTHOR(S): Hoofnagle, Jay H.
CORPORATE SOURCE: Liver Diseases Section, Digestive Diseases Branch, Natl. Inst. Diabetes Digestive Kidney Diseases, Natl. Inst. Health, Bethesda, MD, 20892, USA
SOURCE: Digestion (1998), 59(5), 563-578
CODEN: DIGEBW; ISSN: 0012-2823
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 136 refs. is given. Worldwide hviral hepatitis is the most common cause of jaundice, chronic liver disease cirrhosis and hepatocellular carcinoma. While important advances have been made in prevention of viral hepatitis, therapy of this disease remains unsatisfactory. There are no specific therapies of proven benefit for acute hepatitis, although use of alpha-interferon during the acute phase of hepatitis C may result in a decrease in the rate of chronicity. For chronic viral hepatitis, alpha-interferon has been widely used, but is

expensive, poorly tolerated and limited in effectiveness. New antiviral agents and use of combinations of antivirals are now being evaluated and promise to provide a therapy that is effective in the majority of patients. The currently recommended therapy of chronic hepatitis B is a 4- to 6-mo course of alpha-interferon in doses of 5-10 million units three times a week; a regimen that results in sustained clearance of hepatitis B virus (HBV) DNA and hepatitis B e antigen (HBeAg) from serum in approx. one-third and a loss of hepatitis B surface antigen (HBsAg) in one-tenth of patients. Long-term follow-up of patients who respond to interferon treatment with clearance of HBeAg indicate that the majority ultimately clear HBsAg as well and have continued remission in the liver disease, although low levels of HBV DNA can commonly be detected in liver tissue. Better therapies of hepatitis B are needed. Recently, several oral "second-generation" nucleoside analogs have been developed that have potent activity against HBV. The best studied is lamivudine (3-thiacytidine) which results in marked inhibition of HBV DNA levels and improvement in serum aminotransferases and hepatic histol. in the majority of patients. When stopped, however, most patients relapse and the shortcomings of long-term therapy have been the development of viral resistance in up to one-quarter of patients within a year and a higher percentage with more prolonged therapy. Future approaches of therapy of promise for hepatitis B are combinations of lamivudine with interferon and other antiviral nucleoside analogs. The currently recommended therapy of chronic hepatitis C is a 12- to 18-mo course of alpha interferon in doses of 3 million units three times a week: a regimen that results in sustained clearance of hepatitis C virus (HCV) RNA in approx. 20% of patients. Sustained responses have been assocd. with marked improvements in hepatic histol. and long-term studies indicate that the majority of patients remain free of virus in serum and liver, suggesting a "cure" of infection. Responses to interferon correlate to some degree with clin. and virol. features, including young age, absence of hepatic fibrosis, low levels of HCV RNA in serum and HCV genotypes 2 and 3. Most recently, combinations of alpha interferon and ribavirin, an oral nucleoside analog, have been evaluated and shown to increase the sustained response rate to 30 - 40%. Better therapies are still needed, as the majority of patients with hepatitis C do not have a sustained response to therapy. Extensive research on the mol. structure of HCV indicates several potential means of inhibition of viral replication, including use of protease and helicase inhibitions. What is most needed to advance the field of therapeutics in hepatitis C is development of animal models and cell culture systems with which to study this important viral cause of liver disease.

L22 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:480978 CAPLUS

DOCUMENT NUMBER: 129:254380
TITLE: A one-year trial of lamivudine for chronic hepatitis B
AUTHOR(S): Lai, Ching-Lung; Chien, Rong-Nan; Leung, Nancy W. Y.; Chang, Ting-Tsung; Guan, Richard; Tai, Dar-In; Ng, Keng-Yeen; Wu, Pui-Chee; Dent, Julie C.; Barber, Judy; Stephenson, Sally L.; Gray, D. Fraser
CORPORATE SOURCE: Department of Medicine, Queen Mary Hospital, Hong Kong, Peop. Rep. China
SOURCE: New England Journal of Medicine (1998), 339(2), 61-68
CODEN: NEJMAG; ISSN: 0028-4793
PUBLISHER: Massachusetts Medical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In preliminary trials, lamivudine, an oral nucleoside analog, has shown promise for the treatment of chronic hepatitis B. We conducted a one-year, double-blind trial of lamivudine in 358 Chinese patients with chronic hepatitis B. The patients were randomly assigned to receive 25 mg of lamivudine (142 patients), 100 mg of lamivudine (143), or placebo (73) orally once daily. The patients underwent liver biopsies before entering the study and after completing the assigned treatment regimen. The primary end point was a redn. of at least two points in the Knodell necroinflammatory score. Hepatic necroinflammatory activity improved by two points or more in 56 percent of the patients receiving 100 mg of lamivudine, 49 percent of those receiving 25 mg of lamivudine, and 25 percent of those receiving placebo ($P<0.001$ and $P=0.001$, resp., for the comparisons of lamivudine treatment with placebo). Necroinflammatory activity worsened in 7 percent of the patients receiving 100 mg of lamivudine, 8 percent of those receiving 25 mg, and 26 percent of those receiving placebo. The 100-mg dose of lamivudine was assocd. with a reduced progression of fibrosis ($P=0.01$ for the comparison with placebo) and with the highest rate of hepatitis B e antigen (HBeAg) seroconversion (loss of HBeAg, development of antibody to HBeAg, and undetectable HBV DNA) (16 percent), the greatest suppression of HBV DNA (98 percent redn. at week 52 as compared with the base-line value), and the highest rate of sustained normalization of alanine aminotransferase levels (72 percent). Ninety-six percent of the patients completed the study. The incidence of adverse events was similar in all groups, and there were few serious events. In a one-year study, lamivudine was assocd. with substantial histol. improvement in many patients with chronic hepatitis B. A daily dose of 100 mg was more effective than a daily dose of 25 mg.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 148.90 149.11

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
ENTRY SESSION
CA SUBSCRIBER PRICE -27.01 -27.01

FILE 'STNGUIDE' ENTERED AT 07:42:17 ON 28 APR 2005
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 22, 2005 (20050422/UP).

=> L10 and fibrosis
0 SARS
0 FIBROSIS
L23 0 L10 AND FIBROSIS

=> coronavirus and SARS
0 CORONAVIRUS
0 SARS
L24 0 CORONAVIRUS AND SARS

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.78 149.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
ENTRY SESSION
CA SUBSCRIBER PRICE 0.00 -27.01

FILE 'CAPLUS' ENTERED AT 07:50:06 ON 28 APR 2005
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FILE COVERS 1907 - 28 Apr 2005 VOL 142 ISS 18
FILE LAST UPDATED: 27 Apr 2005 (20050427/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> coronavirus and SARS
2883 CORONAVIRUS
647 CORONAVIRUSES
2966 CORONAVIRUS
(CORONAVIRUS OR CORONAVIRUSES)
1986 SARS
L25 950 CORONAVIRUS AND SARS

=> fibrosis and L25
28868 FIBROSIS
L26 5 FIBROSIS AND L25

=> nucleoside and L25
43410 NUCLEOSIDE
29795 NUCLEOSIDES
54411 NUCLEOSIDE
(NUCLEOSIDE OR NUCLEOSIDES)
L27 15 NUCLEOSIDE AND L25

=> interferon and l25
65244 INTERFERON
67532 INTERFERONS
82016 INTERFERON
(INTERFERON OR INTERFERONS)
L28 66 INTERFERON AND L25

=> side (s) effect
471120 SIDE
79643 SIDES

529621 SIDE
(SIDE OR SIDES)
4334930 EFFECT
2460193 EFFECTS
5613541 EFFECT
(EFFECT OR EFFECTS)
L29 64053 SIDE (S) EFFECT

=> interferon and L29
65244 INTERFERON
67532 INTERFERONS
82016 INTERFERON
(INTERFERON OR INTERFERONS)
L30 1129 INTERFERON AND L29

=> fibrosis and L30
28868 FIBROSIS
L31 34 FIBROSIS AND L30

=> pirfenidone
L32 114 PIRFENIDONE

=> L31 and L32
L33 1 L31 AND L32

=> D IBIB ABS

L33 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:136507 CAPLUS
DOCUMENT NUMBER: 142:238653
TITLE: Combination therapy for treating alphavirus infection and liver fibrosis
INVENTOR(S): Blatt, Lawrence M.
PATENT ASSIGNEE(S): Intermune, Inc., USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005013917	A2	20050217	WO 2004-US5862	20040226

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2003-451316P P 20030228

AB The present invention provides methods for treating alphavirus infections; methods of treating hepatitis C virus (HCV) infections; methods of treating West Nile virus infection; methods of reducing liver fibrosis; methods of increasing liver function in an individual suffering from liver fibrosis; methods of reducing the incidence of complications assocd. with HCV and cirrhosis of the liver; and methods of reducing viral load, or reducing the time to viral clearance, or reducing morbidity or mortality in the clin. outcomes, in patients suffering from viral infection. The methods generally involve administering effective amts. of an interferon receptor agonist and pirfenidone in combination therapy.

=> D L31 IBIB ABS 1-5

L31 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:136507 CAPLUS
DOCUMENT NUMBER: 142:238653
TITLE: Combination therapy for treating alphavirus infection and liver fibrosis
INVENTOR(S): Blatt, Lawrence M.
PATENT ASSIGNEE(S): Intermune, Inc., USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005013917	A2	20050217	WO 2004-US5862	20040226

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-451316P P 20030228

AB The present invention provides methods for treating alphavirus infections; methods of treating hepatitis C virus (HCV) infections; methods of treating West Nile virus infection; methods of reducing liver fibrosis; methods of increasing liver function in an individual suffering from liver fibrosis; methods of reducing the incidence of complications assocd. with HCV and cirrhosis of the liver; and methods of reducing viral load, or reducing the time to viral clearance, or reducing morbidity or mortality in the clin. outcomes, in patients suffering from viral infection. The methods generally involve administering effective amts. of an interferon receptor agonist and pirfenidone in combination therapy.

L31 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:109748 CAPLUS

TITLE: Triple Antiviral Therapy with Amantadine for IFN-Ribavirin Nonresponders with Recurrent Posttransplantation Hepatitis C

AUTHOR(S): Bizollon, Thierry; Adham, Mustapha; Pradat, Pierre; Chevallier, Michelle; Ducerf, Christian; Baulieux, Jacques; Zoulim, Fabian; Trepo, Christian

CORPORATE SOURCE: Hotel-Dieu 1, Lyon, Fr.

SOURCE: Transplantation (2005), 79(3), 325-329
CODEN: TRPLAU; ISSN: 0041-1337

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB BACKGROUND: HCV reinfection after liver transplantation is universal and has an accelerated course with a high risk of progression to cirrhosis. It is now established that combination therapy with interferon (IFN) alpha and ribavirin may achieve a sustained virol. response in 20% of transplanted patients. However, the optimal therapy for nonresponders remains an unresolved issue. We conducted a pilot study to det. the efficacy and safety of triple antiviral therapy in IFN-ribavirin nonresponders with recurrent chronic hepatitis C. METHODS: Twenty-four nonresponders to the IFN-ribavirin combination were enrolled in this pilot study. Patients were treated with IFN-alpha (3 million units three times a week s.c. with ribavirin [800-1,000 mg daily]) and amantadine 200 mg daily for 48 wk. The primary end point was the loss of HCV RNA 6 mo after the end of treatment. RESULTS: Median age was 50 years; 72% were men and 82% had genotype 1. The median interval between the end of combination

therapy and enrollment was 11 mo. Twenty-four patients started therapy, but five (21%) withdrew due to side effects, including two with anemia.On an intent-to-treat basis, 18 patients (75%) had a biochem. response and 9 (37%) had a virol. response at the end of triple antiviral therapy. Eight of these nine patients (33%) had a sustained virol. response. The mean METAVIR score improved from A 2.2 F2.1 before treatment to A 1.2 F1.9 in sustained virol. responders. In virol. nonresponders, inflammatory activity did not change, but fibrosis worsened. Several patients required treatment with erythropoietin for anemia. Triple therapy was well tolerated and neither increased the frequency nor severity of side effects. CONCLUSION: Our results show that triple antiviral therapy for 48 wk induced a sustained virol. response in 33% of IFN-ribavirin nonresponders with recurrent hepatitis C.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1033549 CAPLUS
DOCUMENT NUMBER: 142:758
TITLE: Methods and compositions using immunomodulatory compounds for treatment and management of cancers and other angiogenesis-associated diseases
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103274	A2	20041202	WO 2004-US14004	20040505
WO 2004103274	A3	20050303		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004029832 A1 20040212 US 2003-438213 20030515
WO 2004043377 A2 20040527 WO 2003-US35544 20031106
WO 2004043377 A3 20040805

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-438213 A 20030515
US 2003-704237 A 20031106
US 2002-380842P P 20020517
US 2002-424600P P 20021106

OTHER SOURCE(S): MARPAT 142:758

AB Methods are disclosed for treating, preventing and/or managing cancer, as well as and diseases and disorders assocd. with, or characterized by, undesired angiogenesis. Specific methods encompass the administration of an immunomodulatory compd. alone or in combination with a second active ingredient. The invention further discloses methods for reducing or avoiding adverse side effects assocd. with chemotherapy, radiation therapy, hormonal therapy, biol. therapy or immunotherapy, which comprise the administration of an immunomodulatory compd. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

L31 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:862921 CAPLUS

DOCUMENT NUMBER: 142:112199

TITLE: Recurrent hepatitis C genotype 1b following liver transplantation: treatment with combination interferon-ribavirin therapy

AUTHOR(S): Berenguer, Marina; Prieto, Martin; Palau, Antonio; Carrasco, Domingo; Rayon, Jose-Miguel; Calvo, Felix; Berenguer, Joaquin

CORPORATE SOURCE: Hepato-Gastroenterology Service, Hospital Universitario La Fe, Valencia, 46009, Spain

SOURCE: European Journal of Gastroenterology & Hepatology (2004), 16(11), 1207-1212
CODEN: EJGHES; ISSN: 0954-691X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal
LANGUAGE: English
AB BACKGROUND: Recurrent hepatitis C is very common leading to graft cirrhosis in a significant proportion of patients. Preliminary reports of combination therapy with interferon-ribavirin have been promising but generally applied to selected patients with chronic mild disease. Little is known, however, about the efficacy and risk of adverse effects when it is used in general clin. practice. AIMS: To analyze the efficacy (biochem., virol. and histol. response) and tolerance of combination therapy in patients with recurrent hepatitis C genotype 1b. METHODS: Twenty-four patients (mean age 54 yr; range 37-67 yr; 75% male) with recurrent hepatitis C virus (histol. at baseline: acute hepatitis (n = 3); chronic hepatitis (n = 21) with F3 or 4 in 77%) were treated with 12 mo interferon (1.5-3 MU thrice weekly) + ribavirin (600-1200 mg daily) followed by 6 mo ribavirin (58%), at a median of 427 days (56-2812) after transplantation. RESULTS: Seven patients (29%) discontinued therapy due to side effects, mainly anemia, at a median of 3 mo since initiation. Dose modifications were required in 88% of those completing the whole course of therapy. Overall, the sustained virol. and biochem. response was 12.5%. This rate was slightly higher (18%) if only the 17 patients who finished the whole course of therapy were analyzed. Histol. improvement was achieved in 31.5% of treated patients. CONCLUSIONS: Combination therapy has a very limited efficacy in the liver transplant setting, although some benefit may be achieved, even in those with advanced graft fibrosis. Tolerance, however, remains a matter of concern.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:702397 CAPLUS
DOCUMENT NUMBER: 141:253766
TITLE: Interferon-lamivudine combination is no better than lamivudine alone in anti-HBe-positive chronic hepatitis B
AUTHOR(S): Akarca, Ulus Salih; Ersoz, Galip; Gunsar, Fulya; Karasu, Zeki; Saritas, Elif; Yuce, Gul; Batur, Yucel
CORPORATE SOURCE: Division of Gastroenterology, Ege University Faculty of Medicine, Izmir, Turk.
SOURCE: Antiviral Therapy (2004), 9(3), 325-334
CODEN: ANTHFA; ISSN: 1359-6535
PUBLISHER: International Medical Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background and aims: Results of studies using lamivudine and

interferon combination in the treatment of chronic hepatitis B are not consistent or conclusive. This study aimed to evaluate the efficacy of interferon plus lamivudine use vs. single lamivudine in anti-HBe-pos. chronic hepatitis B. Methods: Eighty patients were treated with either lamivudine or lamivudine plus simultaneously started interferon. Patients were assigned in groups according to random allocation rule. Lamivudine was given 150 mg/day for 96 wk in each group; interferon was administered 10 MU three times a week for 24 wk in the combination therapy group. Results: Alanine aminotransferase (ALT) normalization was achieved earlier in patients treated with lamivudine alone. At the end of treatment, there was no difference between the groups with respect to HBV DNA negativity, ALT normalization and breakthrough rate. Histol. improvement was remarkable in each group, but fibrosis score and necro-inflammatory activity were much lower in lamivudine-treated patients. Conclusions: Addn. of interferon to the lamivudine regimen does not increase the effectiveness of the treatment. Considering the side effects of interferon treatment, this combination seems not to be convenient for anti-HBe-pos. chronic hepatitis B.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L31 IBIB ABS 6-10

L31 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:681518 CAPLUS
DOCUMENT NUMBER: 141:150998
TITLE: Methods for modulating an inflammatory response
INVENTOR(S): Hunter, Christopher; Villarino, Alejandro
PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069173	A2	20040819	WO 2004-US2646	20040130

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,

IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2004069177 A2 20040819 WO 2004-US2767 20040202
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004185049 A1 20040923 US 2004-768744 20040202
PRIORITY APPLN. INFO.: US 2003-444494P P 20030131
US 2003-519074P P 20031110
WO 2004-US2646 A2 20040130

AB The inventive subject matter relates to novel methods for modulating an immune response in an animal, which comprises administering to said animal an effective amt. of an agent that increases IL-27R/WSX-1 activity. Further, the inventive subject matter relates to pharmaceutical compns. comprising an effective amt. of an agent that increases IL-27R/WSX-1 activity.

L31 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:677483 CAPLUS
DOCUMENT NUMBER: 142:169007
TITLE: Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for treatment of HIV/HCV co-infected patients
AUTHOR(S): Laguno, Montserrat; Murillas, Javier; Blanco, Jose Luis; Martinez, Esteban; Miquel, Rosa; Sanchez-Tapias, Jose M.; Bargallo, Xavier; Garcia-Criado, Angeles; Lazzari, Elisa de; Larrousse, Maria; Leon, Agathe; Lonca, Montserrat; Milinkovic, Ana; Gatell, Josep M.; Mallolas, Josep
CORPORATE SOURCE: Infectious Diseases Unit, the Pathology Service, Hospital Clinic Universitari de Barcelona-IDIBAPS,

University of Barcelona, Spain
SOURCE: AIDS (London, United Kingdom) (2004), 18(13), F27-F36
CODEN: AIDSET; ISSN: 0269-9370
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB BACKGROUND: Current therapies for chronic hepatitis C virus (HCV) in HIV co-infected patients have a low success rate and are poorly tolerated. We have evaluated the efficacy and safety of interferon alfa-2b (IFN) + ribavirin (RBV) vs. pegylated interferon alfa-2b (PEG-INF) + RBV. METHODS: Randomized, single-center, open-label clin. trial including patients with: detectable HCV-RNA, alanine aminotransferase > 1.5-fold upper limit of normal, abnormal liver histol., CD4 cell count > 250.times.10/l and HIV RNA < 10 000 copies/mL. Patients were assigned to INF (3.times.10 units three times/wk) or PEG-IFN (100-150 .mu.g/wk) plus RBV (800-1200 mg/day). Duration of treatment was 48 wk (only 24 wk for HCV genotypes 2 or 3 and baseline HCV RNA < 800 000 IU/mL). The primary endpoint was a sustained virol. response (SVR). RESULTS: Ninety-five patients were randomized (43 INF + RBV, 52 PEG-INF + RBV), 68% males, 82% injecting drug users; 63% genotypes 1 or 4 and 36% genotypes 2 or 3; 62% fibrosis index grade .gtoreq.2 and 30% bridging fibrosis/cirrhosis. SVR was significantly higher in the PEG-INF + RBV arm, 44% vs. 21% (intent to treat; P = 0.017). Among patients with genotypes 1 or 4, SVR were 38% vs. 7% (P = 0.007) and 53% vs. 47% (P = 0.730) for genotypes 2 or 3. CD4 cell count but not its percentage dropped in both arms and HIV RNA viral load did not change from baseline. Side effects were very frequent in both arms leading to treatment discontinuation in 14 patients without statistical differences between arms (P = 0.565). CONCLUSION: PEG-INF + RBV was significantly more effective than INF + RBV for the treatment of chronic hepatitis C in HIV co-infected patients, mainly of genotype 1 or 4.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:428800 CAPLUS
DOCUMENT NUMBER: 140:417925
TITLE: Methods and compositions using selective cytokine inhibitory drugs for treatment and management of cancers and other diseases
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043378	A2	20040527	WO 2003-US35545	20031106
WO 2004043378	A3	20040902		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-424601P P 20021106
OTHER SOURCE(S): MARPAT 140:417925

AB Methods for treating, preventing and/or managing cancer as well as and diseases and disorders assocd. with, or characterized by, undesired angiogenesis are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug alone or in combination with a second active ingredient. The invention further discloses methods for reducing or avoiding adverse side effects assocd. with chemotherapy, radiation therapy, hormonal therapy, biol. therapy or immunotherapy which comprise the administration of a selective cytokine inhibitory drug. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

L31 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:233259 CAPLUS
DOCUMENT NUMBER: 140:269294
TITLE: A randomized trial of a 4- vs. 12-week daily interferon dose regimen combined with ribavirin in treatment of patients with chronic hepatitis C
AUTHOR(S): Sarin, Shiv K.; Goyal, Ankur; Kumar, Sudheer; Guptan, Rajkumar C.; Hashmi, Abid Zaffar; Sakhuja, Pooja; Malhotra, Veena
CORPORATE SOURCE: Department of Gastroenterology, G. B. Pant Hospital, New Delhi, 110002, India
SOURCE: Hepatobiliary & Pancreatic Diseases International (2004), 3(1), 42-48

CODEN: HPDIAJ; ISSN: 1499-3872
PUBLISHER: First Affiliated Hospital, Zhejiang University School of Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English
AB BACKGROUND: Std. combination-therapy of ribavirin with alternate day interferon (IFN) in patients with chronic hepatitis C (CHC) has been reported to achieve 30-55% sustained viral response. Early redn. of viral load by daily dosage of IFN could enhance viral clearance. However, the duration of daily dosage protocol and the likely side-effects have not been well studied. The authors compared the efficacy and safety of a 4- vs. 12-wk daily IFN dosage in patients with CHC. METHODS: Fifty-nine, histol. proven CHC patients having ALT levels >1.5 .times. ULN were divided randomly into 2 groups, group I was given IFN 3 MIU daily for 4 wk, followed by tiw up to 12 mo and group II was given IFN 3 MIU daily for 12 wk, followed by tiw up to 12 mo. Ribavirin was given in a dose of 800-1200 mg/d for 12 mo. RESULTS: Fifty-two of the 59 patients (group I = 28; group II = 24) completed the study. The pretreatment variables and the prevalence of HCV genotype 1 were comparable between the groups. Nine patients (29%) in group I and 6 (25%) in group II had stage 3, 4 fibrosis. At the end of 4, 12, 24 and 52 wk, HCV RNA negativity was obsd. in 27%, 54%, 65% and 71% in group I and 38%, 54%, 71% and 75% in group II, resp. (P = ns). Four of the eight (50%) patients with genotype 1 and 30 (69.8%) of 43 patients with genotype non-1 responded to therapy (P=ns). Sustained viral response was achieved in 61% and 71% in groups I and II, resp. None of the variables predicted nonresponse precisely. No serious adverse effects were obsd. and they were comparable between the two groups. CONCLUSION: Daily IFN dosage with ribavirin is safe and can achieve response in up to 65% patients. Since the efficacy of a 4-wk daily dosage of IFN is comparable to a 12-wk schedule, the authors recommend the former regimen.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:13218 CAPLUS
DOCUMENT NUMBER: 140:70552
TITLE: Imatinib mesylate in idiopathic and postpolycythemic myelofibrosis
AUTHOR(S): Hasselbalch, Hans Carl; Bjerrum, Ole Weiss; Jensen, Bjarne Anker; Clausen, Nielsaage Toffner; Hansen, Per Boye; Birgens, Henrik; Therkildsen, Marianne Hamilton; Ralfkiaer, Elisabeth
CORPORATE SOURCE: Department of Medicine, Division of Hematology and Oncology, Roskilde Hospital, Roskilde, 4000, Den.

SOURCE: American Journal of Hematology (2003), 74(4), 238-242
CODEN: AJHEDD; ISSN: 0361-8609
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Imatinib mesylate targets the ATP-binding sites of the protein tyrosine kinase domains assocd. with Bcr-abl, the platelet-derived growth factor (PDGF) and c-kit. In idiopathic myelofibrosis (IMF) PDGF is considered to be one of the growth factors responsible for the development of bone marrow fibrosis. Recently, it has been shown that imatinib has antifibrogenic effect on bone marrow fibrosis in chronic myelogenous leukemia. Treatment with imatinib alone in IMF has been assocd. with significant side effects. In this study, the safety and efficacy of imatinib therapy in IMF, either administered as a single agent or in combination with hydroxyurea (HU) and/or alpha-interferon (IFN-.alpha.) are evaluated. Eleven patients (median age, 63 yr; range, 33-82 yr) with IMF (n = 8) or postpolycythemic myelofibrosis (PPMF) (n = 3) were studied. All patients had been treated with HU (n = 9) and/or IFN (n = 7) before study entry. In all but one patient, treatment with these agents was discontinued when imatinib therapy was instituted. One patient continued IFN when treatment with imatinib was started. Imatinib was given at a dose of 400 mg/day. Nine patients were in an advanced disease phase. The patients have been followed for a median period of 2 mo (range, 0.5-12 mo). Treatment with imatinib has been stopped in six patients (55%), because of overt side effects (n = 4), recurrence of transitory dizziness and visual defects owing to a rising platelet count (n = 1), or the occurrence of an acute subdural hemorrhage that was evacuated without neurol. deficits (n = 1). In nine patients imatinib treatment was followed by a rise in leukocyte and platelet counts that required combination with HU or IFN. The combined treatment modalities were followed by a rapid decrease in cell counts and were well tolerated apart from IFN side effects. A beneficial effect of imatinib was documented in three patients. It is concluded that leukocytosis and thrombocytosis are seen in most patients with myelofibrosis during treatment with imatinib. Combination therapy with HU or IFN seems safe and well tolerated and followed by a decrease in disease activity. A subgroup of patients in an early disease phase might benefit from imatinib therapy alone.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L31 IBIB ABS 11-20

L31 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:10778 CAPLUS
DOCUMENT NUMBER: 140:58174
TITLE: Does interferon-.gamma. improve pulmonary function in idiopathic pulmonary fibrosis?
AUTHOR(S): Prasse, A.; Mueller, K.-M.; Kurz, C.; Hamm, H.; Virchow, J. C., Jr.
CORPORATE SOURCE: Dept of Pneumology, University Clinic, Freiburg, D-79106, Germany
SOURCE: European Respiratory Journal (2003), 22(6), 906-911
CODEN: ERJOEI; ISSN: 0903-1936
PUBLISHER: European Respiratory Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Idiopathic pulmonary fibrosis (IPF) is a disease with progressive and devastating deterioration of lung function and a fatal prognosis, despite aggressive therapeutic attempts, which, in the majority of cases are futile. Recently, a preliminary study of long-term treatment with interferon (IFN).gamma.1b and low-dose prednisolone in patients with IPF suggested that IFN-.gamma.1b treatment may improve lung function parameters of patients with IPF. Ever since, specialists in respiratory medicine who treat patients with IPF, are called by patients demanding treatment with IFN-.gamma.1b. Therefore, the authors here present another prospective investigation of IFN-.gamma.1b in five patients with IPF. According to the previously published design, patients received 200 .mu.g IFN-.gamma.1b s.c. three-times per wk and 10 mg prednisolone orally for 12 mo. Two patients stopped IFN-.gamma.1b treatment after 4 mo due to side-effects and further lung function deterioration and one patient died 3 mo after commencement of therapy. In total, pulmonary function improved in only one patient during IFN-.gamma.1b treatment, while four patients deteriorated. To conclude, this small series of idiopathic pulmonary fibrosis cases treated with interferon-.gamma.1b and corticosteroids does not support previous data that this treatment improves pulmonary function or alters the natural course of idiopathic pulmonary fibrosis. Furthermore, in the authors' experience, side-effects of interferon-.gamma.1b treatment can significantly reduce patients' quality of life.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:991351 CAPLUS
DOCUMENT NUMBER: 140:23246
TITLE: Combination treatments for purinoceptor-related

disorders
INVENTOR(S): Wilson, Constance N.; Sirgo, Mark A.
PATENT ASSIGNEE(S): Endacea, Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003103675	A2	20031218	WO 2003-US17964	20030606
WO 2003103675	A3	20040325		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-386769P P 20020606
OTHER SOURCE(S): MARPAT 140:23246
AB The present invention provides methods of preventing and treating purinoceptor-related disorders comprising concurrently administering an A1 adenosine receptor antagonist or a P2x purinoceptor antagonist with an at least one addnl. active agent effective to treat purinoceptor-related disorders. The present invention also provides pharmaceutical formulations suitable for preventing and treating purinoceptor-related disorders. Blocking activation of purinergic receptors may be effective for the prevention and early treatment of allergic asthma (both bronchoconstriction and innflammation) without the side effects assocd. with many current therapies.

L31 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:634732 CAPLUS
TITLE: Structure activity relationship studies and pharmacological evaluation of 3,5-disubstituted thiophene-2-carboxylic acid derivatives: Potent inhibitors of HCV NS5B polymerase and HCV subgenomic RNA replication
AUTHOR(S): Poisson, Carl; Chan, Laval; Das, Sanjoy Kumar; Reddy, Thumkunta J.; Pereira, Oswy Zeno; Proulx, Melanie;

Halab, Liliane; Courchesne, Marc; Roy, Caroline; Yannopoulos, Constantin; Siddiqui, Arshad; Wang, Wuyi; Nguyen-Ba, Nghe P.; Zhang, Ming-Qiang; Bethell, Richard; L'Heureux, Lucille; David, Maud; Bedard, Jean; Hamel, Martine; Bilimora, Darius; Nicolas, Olivier; Morin, Nicolas; Asselin, Philippe; Hamelin, Bettina; Dong, Kelly; Rioux, Nathalie; Richard, Annie; James, Michael N. G.; Wang, Meitian; Ng, Kenneth K.-S.; Cherney, Maia M.

CORPORATE SOURCE: Department of Medicinal Chemistry, Shire BioChem Inc, Laval, QC, H7V 4A7, Can.

SOURCE: Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), MEDI-124. American Chemical Society: Washington, D. C.
CODEN: 69EKY9

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Hepatitis C Virus (HCV) is a blood-borne pathogen and has infected approx. 170 million people worldwide. Close to 60% of these infected people develop a chronic infection that leads to cirrhosis, fibrosis and in some cases, to hepatocellular carcinoma. It is estd. that by the year of 2010, the total deaths from HCV-related disease may overtake the current death toll due to AIDS. So far the only available therapy requires the use of interferon-a in conjunction with ribavirin. The utility of this therapy is limited by serious side effects and low response against HCV genotype 1. Therefore, there remains a significant unmet medical need for a safe and well-tolerated oral therapy for the treatment of HCV. Of several attractive viral enzyme targets, the RNA-dependent RNA polymerase has been shown to be crit. for viral replication; thus this enzyme represents an important target for the discovery of novel antiviral agents. Recently, we have discovered a novel class of 3,5-disubstituted thiophene-2-carboxylic acid derivs. as HCV NS5B polymerase inhibitors. Structure activity relationship studies were then undertaken and have yielded several potent inhibitors. This poster will outline the detailed SAR studies, pharmacol. and biol. evaluation of these thiophene-2-carboxylic acid derivs. as potent inhibitors of HCV NS5B polymerase as well as of HCV subgenomic RNA replication.

L31 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:536735 CAPLUS

DOCUMENT NUMBER: 139:143587

TITLE: Pegylated interferon alpha-2b plus ribavirin after OLT: Sustained virological response (SVR), clinical course and histology

AUTHOR(S): Bahra, M.; Neumann, U. P.; Berg, T.; Neuhaus, R.;

Langrehr, J. M.; Neuhaus, P.
CORPORATE SOURCE: Department of Surgery, Charite Campus Virchow-Clinic, Humboldt-University, Berlin, Germany
SOURCE: Chirurgisches Forum fuer Experimentelle und Klinische Forschung (2003) 345-347
CODEN: CFEKA7; ISSN: 0303-6227
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Recurrence of hepatitis C (HCV) infection after OLT for HCV cirrhosis is almost universal and approx. 10% of patients develop cirrhosis after OLT for HCV. Common treatments with ribavirin and interferon alpha-2b failed to show a satisfying sustained antiviral response (SVR). Peg-Intron is a pegylated form of interferon alpha-2b and has been proved to increase the response of antiviral therapy in non-transplanted HCV pos. patients. The aim of this prospective open non-randomized trial was to examine whether Peg-Intron in combination with ribavirin is effective to treat liver transplant recipients with HCV reinfection. 25 Patients with pos. HCV RNA and histol. proven hepatitis C reinfection after OLT for HCV cirrhosis received peginterferon alpha-2b plus ribavirin for 48 wk (Peg-Intron 1 - 1,5 .mu.g/kg/wk plus ribavirin 200 - 800 mg/d). We assessed efficacy by HCV RNA and ALT response. Liver biopsies were performed routinely at start of treatment and 24 wk after end of treatment. Antiviral response was defined as undetectable HCV RNA in serum at the end of follow-up. Biochem. response was defined as normalization of serum alanine aminotransferase (ALT). Histol. findings were scored for inflammation/fibrosis and histol. changes between liver biopsies prior treatment and 6 mo after cessation of treatment were compared. The primary endpoint was defined as sustained virol. response (SVR) 24 wk after end of treatment. After a median treatment period of 48 wk in 18/25 (72%) patients HCV RNA was not longer detectable. The primary endpoint, a sustained virol. response (SVR) at the end of a 24-wk follow-up (week 72), was obsd. in 9/25 patients (36%). Comparisons of histol. findings for inflammation and fibrosis showed no degrdn. during treatment. Side effects were neutropenia 15/25 (60%), anemia 5/25 (20%), psychiatric disorders 2/25 (8%), fever, vertigo, shivers and headache 12/25 (48%). Side effects were treated with dose redn. and 30 Mio IU GM-CSF twice a week to manage neutropenia. For patients with chronic hepatitis C reinfection after liver transplantation the combination of pegylated interferon alpha-2b plus ribavirin is effective and save. 36% Of the patients showed a sustained virol. response. No degrdn. of histol. findings were seen during treatment. Peginterferon plus ribavirin seems to improve the clin. course and outcome of HCV reinfection after OLT.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:515824 CAPLUS
DOCUMENT NUMBER: 139:66936
TITLE: Hepatitis C and liver fibrosis
AUTHOR(S): Schuppan, D.; Krebs, A.; Bauer, M.; Hahn, E. G.
CORPORATE SOURCE: Department of Medicine I, University of Erlangen-Nuernberg, Germany
SOURCE: Cell Death and Differentiation (2003), 10(1, Suppl. 1), S59-S67
CODEN: CDDIEK; ISSN: 1350-9047
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Chronic hepatitis C progresses to cirrhosis within 20 yr in an estd. 20-30% of patients, while running a relatively uneventful course in most others. Certain HCV proteins, such as core and NS5A, can induce derangement of lipid metab. or alter signal transduction of infected hepatocytes which leads to the prodn. of reactive oxygen radicals and profibrogenic mediators, in particular TGF-.beta.1. TGF-.beta.1 is the strongest known inducer of fibrogenesis in the effector cells of hepatic fibrosis, i.e. activated hepatic stellate cells and myofibroblasts. However, fibrogenesis proceeds only when addnl. profibrogenic stimuli are present, e.g. alc. exposure, metabolic disorders such as non-alc. steatohepatitis, or coinfections with HIV or Schistosoma mansoni that skew the immune response towards a Th2 T cell reaction. Furthermore, profibrogenic polymorphisms in genes that are relevant during fibrogenesis have been disclosed. This knowledge will make it possible to identify those patients who are most likely to progress and who need antiviral or antifibrotic therapies most urgently. However, even the best available treatment, the combination of pegylated interferon and ribavirin, which is costly and fraught with side effects , eradicates HCV in only 50% of patients. While the suggestive antifibrotic effect of interferons (IF-.gamma. > .alpha.,.beta.), irresp. of viral elimination, has to be proven in randomized prospective studies, addnl., well tolerated and cost-effective antifibrotic therapies have to be developed. The combination of cytokine strategies, e.g. inhibition of the key profibrogenic mediator TGF-.beta., with other potential antifibrotic agents appears promising. Such adjunctive agents could be silymarin, sho-saiko-to, halofuginone, phosphodiesterase inhibitors, and endothelin-A-receptor or angiotensin antagonists. Furthermore, drug targeting to the fibrogenic effector cells appears feasible. Together with the evolving validation of serol. markers of hepatic fibrogenesis and fibrolysis an effective and individualized treatment of liver fibrosis is anticipated.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:425549 CAPLUS
DOCUMENT NUMBER: 139:116055
TITLE: Efficacy of interferon-.alpha. treatment in Japanese children with chronic hepatitis C
AUTHOR(S): Nakashima, Eisuke; Fujisawa, Takuji; Kimura, Akihiko; Kage, Masayoshi; Yamato, Yasuhiko; Maeda, Kohji; Kumagai, Masami; Ushijima, Kosuke; Yamashita, Yasuhiro; Matsuishi, Toyojiro
CORPORATE SOURCE: Departments of Pediatrics and Child Health, Kurume University School of Medicine, Kurume, Japan
SOURCE: Journal of Gastroenterology and Hepatology (2003), 18(4), 411-414
CODEN: JGHEEO; ISSN: 0815-9319
PUBLISHER: Blackwell Publishing Asia Pty Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We investigated the efficacy of natural interferon (IFN)-.alpha. treatment in 34 Japanese children with chronic hepatitis C. Thirty-four children completed 6 mo of therapy with natural IFN-.alpha. and were followed for 12 mo or longer. We examd. the serum hepatitis C virus (HCV) RNA titer and liver histol. before, during, and after IFN treatment. At 6 mo after the cessation of IFN-.alpha. treatment, 16 patients (47%) had normal serum alanine aminotransferase concn. and no detectable serum HCV RNA. There were no major side-effects, excluding some influenza-like symptoms during the IFN-.alpha. treatment. Most genotype 2a patients had a complete response (80%). Moreover, patients who had a low HCV RNA titer (<102 copies/mL) after 1 mo of IFN-.alpha. treatment became complete responders at 6 mo after the cessation of treatment. Histol. improvement was obsd. in almost all patients after IFN-.alpha. treatment. Interferon-.alpha. treatment is safe and effective for children with chronic hepatitis C and has no serious side-effects. A HCV RNA concn. of <102 copies/mL after 1 mo of IFN-.alpha. treatment and genotype 2a may be useful predictors of long-term IFN efficacy.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:120034 CAPLUS
DOCUMENT NUMBER: 138:219893

TITLE: Interferons and their application in the diseases of the lung
AUTHOR(S): Antoniou, Katerina M.; Ferdoutsis, Emmanouil; Bouros, Demosthenes
CORPORATE SOURCE: Interstitial Lung Disease Unit, Department of Pneumonology, Medical School University of Crete, Univ. Hospital, Crete, Greece
SOURCE: Chest (2003), 123(1), 209-216
CODEN: CHETBF; ISSN: 0012-3692
PUBLISHER: American College of Chest Physicians
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Interferons (IFNs) are a family of cytokine mediators that are critically involved in alerting the cellular immune system to viral infections of host cells. There are three major classes of IFNs, as follows: IFN-.alpha.; IFN-.beta.; and IFN-.gamma.. IFNs are being investigated and applied in various respiratory disorders, including interstitial lung diseases, lung cancer, malignant mesothelioma, malignant pleural effusions, and respiratory infections. Recent promising preliminary results concerning patients with idiopathic pulmonary fibrosis who have been treated with IFN-.gamma.1b should prompt the performance of further confirmatory well-designed multicenter trials. IFN-.gamma. is emerging as an important cytokine for use in the treatment of patients with infectious diseases, including multidrug-resistant pulmonary TB. A better understanding of IFN biol., indications, side effect profiles, and toxicity management will aid in optimizing its use in the treatment of patients. The purpose of this article is, therefore, to review the current clin. use of IFNs in the treatment of patients with respiratory diseases.
REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:789947 CAPLUS
DOCUMENT NUMBER: 137:304330
TITLE: The efficacy of a herbal medicine (Mao-to) in combination with intravenous natural interferon-.beta. for patients with chronic hepatitis C, genotype 1b and high viral load: a pilot study
AUTHOR(S): Kainuma, M.; Ogata, N.; Kogure, T.; Kohta, K.; Hattori, N.; Mitsuma, T.; Terasawa, K.
CORPORATE SOURCE: Department of Japanese Oriental Medicine, Toyama Medical and Pharmaceutical University, Toyama, Japan
SOURCE: Phytomedicine (2002), 9(5), 365-372

CODEN: PYTOEY; ISSN: 0944-7113
PUBLISHER: Urban & Fischer Verlag GmbH & Co. KG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Patients with chronic hepatitis C, with a high serum viral load (.gtoreq. 1Meq/mL) and genotype 1b seem to be resistant to interferon (IFN)therapy. To evaluate the efficacy of a herbal medicine (Mao-to) in combination with natural IFN-.beta. for the treatment of these patients, eighteen Japanese patients were enrolled in this study. Every patient received 6 million units (MU) of IFN-.beta. i.v. daily for 8 wk. Mao-to was given orally 3-4 times a day during the IFN-.beta. administration, Sixteen of the 18 patients (89 %) became neg. for serum HCV RNA at the end of treatment, but only 2 of them (11%) remained neg. for the virus RNA at 6 mo of follow-up. Serum ALT levels normalized in 17 patients (94%) at 2 wk of follow-up after the cessation of therapy, and 11 patients (61%) retained normal ALT levels for more than 6 mo of follow-up. This rate of biochem. response was high as compared with that of therapy with IFN-.beta. alone (19%) in the largest IFN-.beta. trial in Japan. Serum hyaluronic acid levels were decreased significantly from 147.0.+-.110.5 ng/mL to 77.4.+-.67.4 ng/mL in the sustained biochem. response group (P = 0.003). None of the patients needed to interrupt therapy because of side effects of IFN-.beta.. Thus, Mao-to administration together with IFN-.beta. treatment could increase the sustained biochem. response rate, and reduce liver fibrosis.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:754190 CAPLUS
DOCUMENT NUMBER: 137:257653
TITLE: Nicotinic receptor agonists for the treatment of inflammatory diseases
INVENTOR(S): Cormier, Yvon; Israel-Assayag, Evelyne; Blanchet, Marie-Renee
PATENT ASSIGNEE(S): Universite Laval, Can.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002076434	A2	20021003	WO 2002-CA412	20020325

WO 2002076434 A3 20030717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2341952 AA 20020923 CA 2001-2341952 20010323
CA 2441096 AA 20021003 CA 2002-2441096 20020325
EP 1370264 A2 20031217 EP 2002-717896 20020325
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
BR 2002008305 A 20040309 BR 2002-8305 20020325
JP 2004523588 T2 20040805 JP 2002-574950 20020325
NO 2003004185 A 20031124 NO 2003-4185 20030919
US 2004132737 A1 20040708 US 2004-469999 20040224
PRIORITY APPLN. INFO.: CA 2001-2341952 A 20010323
WO 2002-CA412 W 20020325

AB The invention discloses the use of nicotine receptor agonists for treating inflammatory diseases, including a variety of pulmonary diseases. Such agonists have fewer side effects than other antiinflammatory drugs, e.g. steroids. Moreover, these agonists can be used alone or in combination with other antiinflammatory drugs to alleviate pulmonary diseases.

L31 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:713949 CAPLUS
DOCUMENT NUMBER: 137:241990
TITLE: Clinical observation of salvianolic acid B in treatment of liver fibrosis in chronic hepatitis B
AUTHOR(S): Liu, Ping; Hu, Yi-Yang; Liu, Cheng; Zhu, Da-Yuan; Xue, Hui-Ming; Xu, Zhi-Qiang; Xu, Lie-Ming; Liu, Cheng-Hai; Gu, Hong-Tu; Zhang, Zhi-Qing
CORPORATE SOURCE: Shanghai University of Traditional Chinese Medicine, Shanghai, 200032, Peop. Rep. China
SOURCE: World Journal of Gastroenterology (2002), 8(4), 679-685
CODEN: WJGAF2; ISSN: 1007-9327
PUBLISHER: World Journal of Gastroenterology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this study was to evaluate the clin. efficacy of salvianolic acid B (SA-B) on liver fibrosis in chronic hepatitis B. Sixty patients with definite diagnosis of liver fibrosis with hepatitis B were included in the trial. Interferon-.gamma. (IFN-.gamma.) was used as control drug. The patients took orally SA-B tablets or received muscular injection of IFN-.gamma. in the double blind randomized test. The complete course lasted 6 mo. The histol. changes of liver biopsy specimen before and after the treatment were the main evidence in evaluation, in combination with the results of contents of serum HA, LN, IV-C, P-III-P, liver ultrasound imaging, and symptoms and signs. Reverse rate of fibrotic stage was 36.67 % in SA-B group and 30.0 % in IFN-.gamma. group. Inflammatory alleviating rate was 40.0 % in SA-B group and 36.67 % in IFN-.gamma. group. The av. content of HA and IV-C was significantly lower than that before treatment. The abnormal rate also decreased remarkably. Overall anal. of 4 serol. fibrotic markers showed significant improvement in SA-B group as compared with the IFN-.gamma. group. Score of liver ultrasound imaging was lower in SA-B group than in IFN-.gamma. group (HA 36.7 % vs. 80 %, IV-C 3.3 % vs. 23.2 %). Before the treatment, ALT AST activity and total bilirubin content of patients who had regression of fibrosis after oral administration of SA-B, were significantly lower than those of patients who had aggravation of fibrosis after oral administration of SA-B. IFN-.gamma. showed certain side effects (fever and transient decrease of leukocytes, occurrence rates were 50 % and 3.23 %), but SA-B showed no side effects. SA-B could effectively reverse liver fibrosis in chronic hepatitis B. SA-B was better than IFN-.gamma. in redn. of serum HA content, overall decrease of 4 serum fibrotic markers, and decrease of ultrasound imaging score. Liver fibrosis in chronic hepatitis B with slight liver injury was more suitable to SA-B in anti-fibrotic treatment. SA-B showed no obvious side effects.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L31 IBIB ABS 21-34

L31 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:659617 CAPLUS
DOCUMENT NUMBER: 137:210290
TITLE: Use of modulators of airways inflammation in patients with CF
AUTHOR(S): Ren, Clement L.
CORPORATE SOURCE: Division of Pediatric Pulmonology & Allergy, University of Rochester, Rochester, NY, 14642, USA

SOURCE: Clinical Reviews in Allergy & Immunology (2002), 23(1), 29-39
CODEN: CRAIF2; ISSN: 1080-0549
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. One of the hallmarks of cystic fibrosis (CF) lung disease is the presence of intense, neutrophil-dominated airway inflammation, and many researchers have focused on developing therapies to reduce inflammation in CF lung disease. Systemic corticosteroids can delay progression of lung disease, but at the cost of unacceptable side effects. Inhaled corticosteroids are widely used, but their efficacy has yet to be demonstrated in a controlled fashion. Ibuprofen has also been shown to delay disease progression, but its use has been limited by the need to obtain individual pharmacokinetics and concern about side effects. Other treatments with potential anti-inflammatory effects include pentoxifylline, leukotriene antagonists, docosahexaenoic acid, and azithromycin. Few, if any, large clin. studies of these therapies have been published, but several are presently underway. Because neutrophil elastase appears to be a key mediator of tissue damage in CF lung disease, anti-elastase compds. have also been studied, including alpha-1-protease inhibitor, secretory leukocyte protease inhibitor, and small mol. inhibitors. There have been no large-scale controlled trials of these therapies in CF. More recently, investigators have focused on cytokine modulation, using either interleukin-10 or interferon gamma. Some complementary and alternative medicine therapies may also have anti-inflammatory effects, although their clin. value has yet to be demonstrated in a rigorously-controlled fashion. In summary, numerous anti-inflammatory therapies have been applied to CF lung disease, but more large, well-controlled studies will need to be performed to det. their true clin. usefulness.
REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:781966 CAPLUS
DOCUMENT NUMBER: 136:384688
TITLE: The effects of intravenous and intramuscular high dose interferon therapy on hepatitis C virus dynamics
AUTHOR(S): Sakamoto, Masafumi
CORPORATE SOURCE: Third Department of Internal Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan
SOURCE: Kyoto-furitsu Ika Daigaku Zasshi (2001), 110(9),

865-876
CODEN: KFIZAO; ISSN: 0023-6012
PUBLISHER: Kyoto-fu Igaku Shinkokai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB This study aimed to clarify the clin. significance of hepatitis C virus (HCV) turnover in chronic hepatitis C (CH-C) patients receiving interferon (IFN) .alpha. i.v. (IV-group) or i.m. (IM-group). In 28 CH-C patients (14; IV-group, 14; IM-group) receiving 10 MU of 1FN.alpha. daily, the serum amt. of HCV RNA, HCV genotype, amino acid sequence in NSSA (genotype 1b), and the stage of liver disease were evaluated before therapy. Blood samples were taken before, 3, 6, 12, 24 h and 2, 4, 7, 14 days after the initial IFN administration, and used for the anal. of the half-life of HCV. The half life of HCV turnover was significantly shorter in the IV-group than in the IM-group (5.5.+-.1.8 h v.s. 8.3.+-.7.1 h) within the first 24 h (first phase). The first phase was significantly shorter in genotype HCV-2 patients in the IV-group, but no significant relations were noted among the half-life of HCV turnover and serum HCV RNA level, grade of fibrosis and amino acid sequence in NSSA. No significant differences were noted in side effects between IM- and IV-groups. The dynamics of HCV turnover within 24 h was influenced by administration route and HCV genotype.

L31 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:763235 CAPLUS
DOCUMENT NUMBER: 135:314399
TITLE: Detection of variations in the DNA methylation profile of genes in the determining the risk of disease
INVENTOR(S): Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander
PATENT ASSIGNEE(S): Epigenomics A.-G., Germany
SOURCE: PCT Int. Appl., 636 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 68
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077373	A2	20011018	WO 2001-DE1486	20010406

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
DE 10019058 A1 20011220 DE 2000-10019058 20000406
WO 2001077373 A2 20011018 WO 2001-XA1486 20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG
WO 2001077373 A2 20011018 WO 2001-XB1486 20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG
EP 1274865 A2 20030115 EP 2001-953936 20010406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
EP 1278892 A1 20030129 EP 2001-940158 20010406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003531589 T2 20031028 JP 2001-575634 20010406
EP 1360319 A2 20031112 EP 2001-955278 20010406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2004067491 A1 20040408 US 2003-240454 20030311
US 2003162194 A1 20030828 US 2003-240452 20030414
JP 2004008217 A2 20040115 JP 2003-160375 20030605
US 2004023279 A1 20040205 US 2003-455212 20030605
PRIORITY APPLN. INFO.: DE 2000-10019058 A 20000406
DE 2000-10019173 A 20000407
DE 2000-10032529 A 20000630
DE 2000-10043826 A 20000901
WO 2001-DE1486 W 20010406
WO 2001-EP3969 W 20010406
WO 2001-EP4016 W 20010406
EP 2002-90203 A 20020605

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the DNA methylation of a target group of genes. The invention further relates to the use of the same for detg. the gene variant with regard to DNA methylation, a medical device, using an oligonucleotide kit, a method for detg. the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a disease state in an individual. Such diseases may be: undesired pharmaceutical side-effects ; cancerous diseases; CNS dysfunctions, injuries or diseases; aggressive symptoms or relational disturbances; clin., psychol. and social consequences of brain injury; psychotic disorders and personality disorders; dementia and/or assocd. syndromes; cardiovascular disease, dysfunction and damage; dysfunction, damage or disease of the gastrointestinal tract; dysfunction, damage or disease of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; dysfunction, damage or disease of the body as an abnormal development process; dysfunction, damage or disease of the skin, muscle, connective tissue or bones; endocrine and metabolic dysfunction, damage or disease; headaches or sexual dysfunction. This abstr. record is one of several records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.

L31 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L31 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:895179 CAPLUS

DOCUMENT NUMBER: 135:86910

TITLE: Unfavorable effects of colchicine in combination with interferon-.alpha. in the treatment of chronic hepatitis C

AUTHOR(S): Angelico, M.; Cepparulo, M.; Barlattani, A.; Liuti, A.; Gentile, S.; Hurtova, M.; Ombres, D.; Guarascio, P.; Rocchi, G.; Angelico, F.

CORPORATE SOURCE: Chairs of Gastroenterology Department of Public Health, University of Rome, Tor Vergata, 00133, Italy

SOURCE: Alimentary Pharmacology and Therapeutics (2000), 14(11), 1459-1467
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The prognosis of chronic hepatitis depends on the progression of hepatic fibrosis. To investigate whether the antifibrotic drug colchicine, in combination with interferon-.alpha. has a role in the treatment of chronic hepatitis C. Sixty-five HCV-RNA pos. patients

with chronic hepatitis were randomized to receive interferon -.alpha., 6 MU t.i.w. for 6 mo followed by 3 MU t.i.w. for further 6 mo, with or without the adjunct of colchicine, 1 mg o.d., 6 days a week, for 3 yr. We report an interim anal. after the first 18 mo. Thirty-four patients received interferon-.alpha. and 31 received interferon-.alpha. and colchicine. The two groups were comparable for baseline data, including HCV-RNA levels, genotypes and histol. grading/staging. Drop-outs and side-effects were similar. The proportion of patients who achieved alanine transaminase normalization or undetectable HCV-RNA at month 6 was higher in the interferon-.alpha. (68% and 47%, resp.) than in the interferon-.alpha. plus colchicine group (32% and 23%, P = 0.004 and P = 0.04, resp.). End-of-treatment biochem. and virol. response occurred in 41% and 29% of the interferon-.alpha. and 19% and 10% of the combination group, resp. (P = 0.05 and P = 0.05). Sustained biochem. response occurred in 26% of the interferon-.alpha. and 6% of the interferon-.alpha. plus colchicine group (P = 0.03), corresponding percentages of sustained HCV-RNA loss being 21% and 3% (P = 0.04). The combination of colchicine and interferon-.alpha. worsens the effectiveness of interferon-.alpha. alone in HCV chronic hepatitis. These alarming findings prompted us to interrupt the trial at this stage.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:841769 CAPLUS

DOCUMENT NUMBER: 135:44988

TITLE: Studies of the effectiveness of interferon alpha treatment for chronic hepatitis C in children

AUTHOR(S): Czerwionka-Szaflarska, Mieczyslawa; Chrobot, Andrzej; Szaflarska-Szczepanik, Anna

CORPORATE SOURCE: Chair and Department of Pediatrics, Allergology and Gastroenterology, Medical University, Bydgoszcz, Pol.

SOURCE: Medical Science Monitor (2000), 6(5), 964-970
CODEN: MSMOFR; ISSN: 1234-1010

PUBLISHER: Medical Science International Publishing

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Introduction: The significance of hepatitis C infection in Poland, particularly in a pathol. of the developmental age still increased. The aim of the study was the anal. of interferon alpha therapy efficacy in children with chronic C hepatitis. Material and methods: 30 children (aged from 3 yr to 15 yr, 16 females, 14 males) were included in the study. In each patient HCV infection was confirmed by the serol.,

mol. (with identification of HCV genotype) and histopathol. methods. The duration of observation of HCV-infected children after the diagnosis was made followed for at least 6 mo. Transaminase level in each case was 50% higher than normal. The schema of interferon alpha treatment was: 3 MU 3 times a week s.c. for 25 wk. Time of observation started at the beginning of the therapy and finished 1 yr after the end of the treatment. Results: The anal. of the HCV genotypes showed the predominance of the genotype 1 (66.7%): subtype 1a was found in 20% patients, subtype 1b - in 43.5% children. Genotype 4 (subtype 4c4d or 4b) was confirmed in 30% patients, genotype 3 (subtype 3a) in 3.3% patients. In the histopathol. picture of the liver predominated minimal or moderate inflammation activity (grading: 1 - in 50%, 2 - in 46.6%, 3 - in 3.4%) and little fibrosis (staging: 0 - in 80%, 1 - in 13.3%, 2 - in 6.7%). In many children mild side effects of interferon alpha therapy were obsd.: pseudoinfluenzal symptoms (in 46.7%), lack of appetite (in 16.7%), abdominal pain (in 10%), thrombocytopenia (in 6.7%), granulocytopenia, hair loss, irritability, itching of the skin (in 3.4%). At the end of therapy in 36.7% patients serum HCV-RNA was undetectable. The percentage of children without serum HCV-RNA decreased 6 mo after the end of therapy to 20% patients and a year after the end of therapy to only 13.6% children. In children with HCV-RNA elimination was obsd. early redn. of ALT level. For the definition of the predictive factors of good prognosis patients were divided into 2 groups: group I (without HCV-RNA elimination at the end of the treatment) and group II (patients HCV-RNA neg. a year after the end of therapy). Both group of children were similar in respect of age, disease duration and interferon alpha dosis/m2. At the beginning of the treatment mean ALT level was statistically higher in group II than in group I. IL-2 level was significant higher in group II than at the beginning, after 2 and 4 mo of the therapy. There were no significant differences in IL-1.beta., IL-4 and IL-6 level between patients in group I and II. The differences in ALT activity during IFN-therapy between 2 groups of patients were statistically significant; since second month of therapy higher ALT level was obsd. in a group of patients without HCV-RNA elimination. In the histopathol. picture of the liver a year of the end of therapy in 20% children redn. of inflammatory activity and progression of fibrosis in both group of patients was obsd. Conclusions: Because of a little efficacy, high costs, psychol. load of young patients and possible following consequences of the interferon alpha therapy it is necessary to manage the further researches to find a new method of treatment of chronic C hepatitis. High ALT activity and elevated IL-2 level before treatment seems to be predictive factors of the good response to interferon alpha therapy.

L31 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:652023 CAPLUS
DOCUMENT NUMBER: 134:141380
TITLE: Treatment of chronic hepatitis C with amantadine
AUTHOR(S): Goff, John S.; Reveille, R. Matthew; Johnson, Judy
CORPORATE SOURCE: Rocky Mountain Gastroenterology Associates, Denver, CO, 80007, USA
SOURCE: Digestive Diseases and Sciences (2000), 45(7), 1389-1391
CODEN: DDSCDJ; ISSN: 0163-2116
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hepatitis C is usually treated with interferon or a combination of interferon and ribavirin, but these agents have numerous side effects, and interferon must be given by injection three time a week. An alternative oral medication would be a welcome advance for treating hepatitis C. Amantadine has been reported to have the potential to produce viral suppression in patients with hepatitis C. To gain further knowledge about the effects of amantadine on hepatitis C, we treated 24 patients for 3-12 mo (av. = 5.5 mo; median = 4.5 mo) with 100 mg amantadine twice daily. Twelve patients had stage 3 or 4 fibrosis on biopsy. Eleven patients had a fall in viral titer, but complete viral suppression was not seen in any patient. Three patients had no viral titer obtained after treatment, but their elevated transaminase levels did not change with treatment. Of the 15 patients with a decrease in enzyme levels, only two patients had normalization. Six patients had side effects during the treatment, but in only one was amantadine stopped solely because of side effects. Based on these results and a literature review, we do not believe amantadine is an effective single agent for the treatment of chronic hepatitis C.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:517046 CAPLUS
DOCUMENT NUMBER: 133:260954
TITLE: Treatment of hepatitis C with interferon and ribavirin
AUTHOR(S): Pianko, Stephen; McHutchison, John G.
CORPORATE SOURCE: Division of Gastroenterology/Hepatology, Scripps Clinic and Research Foundation, La Folla, CA, 92037, USA

SOURCE: Journal of Gastroenterology and Hepatology (2000), 15(6), 581-586
CODEN: JGHEEO; ISSN: 0815-9319
PUBLISHER: Blackwell Science Asia Pty Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 29 refs. Hepatitis C is a worldwide problem that frequently results in end-stage liver disease and its complications. Treatment for hepatitis C virus (HCV) has been rather ineffective but several recent studies have clarified the role of interferon and ribavirin therapy. In line with therapeutic progress in HIV infection, hepatitis C is now entering the era of multidrug antiviral therapy. Ribavirin is an orally active synthetic guanosine analog with theor. antiviral and immunomodulatory actions. In this review we have evaluated the role of interferon and ribavirin in treatment-naive patients, relapsers and non-responders. In naive patients the combination results in improved end-of-treatment and sustained response rates, with an overall 41% sustained virol. response rate in patients treated for 48 wk. Therapeutic benefit also extends to the traditionally difficult to treat patients (genotype 1, high viral load and advanced fibrosis). The addn. of ribavirin to interferon has also resulted in an increased toxicity profile, which has made therapy more difficult for both the patient and managing physician. However, the significant improvement in response rates for all patients makes combination therapy the most appropriate choice as the first-line therapy for suitable patients with chronic viral hepatitis C. Appropriate management with interferon and ribavirin includes assessing the patient's HCV genotype to det. the optimal duration of therapy, assessing therapeutic efficacy by measuring HCV-RNA at 24 wk and monitoring for the addnl. ribavirin side-effects.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:122895 CAPLUS
DOCUMENT NUMBER: 132:160875
TITLE: Pilot study of combination therapy with ribavirin and interferon alfa for the retreatment of chronic hepatitis B e antibody-positive patients
AUTHOR(S): Cotonat, Teresa; Quiroga, Juan Antonio; Lopez-Alcorocho, Juan Manuel; Clouet, Rosa; Pardo, Margarita; Manzarbeitia, Felix; Carreno, Vicente
CORPORATE SOURCE: Departments of Hepatology, Fundacion Jimenez Diaz, Madrid, 28040, Spain
SOURCE: Hepatology (Philadelphia) (2000), 31(2), 502-506

CODEN: HPTLD9; ISSN: 0270-9139
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Twenty-four patients with chronic hepatitis B virus (HBV), antibody to hepatitis B e antigen (anti-HBe), HBV DNA positivity, and alanine transaminase (ALT) elevation who failed previous interferon alfa (IFN-.alpha.) therapy were included in a pilot study of combination therapy with ribavirin and IFN-.alpha.. The patients received daily oral ribavirin (1,000-1,200 mg according to body wt.) plus 5 million units (MU) IFN-.alpha.2b three times a week for 12 mo and were followed-up for 12 mo. The median viremia level decreased significantly at the end of treatment (1.2.times.103 copies/mL) and follow-up (4.0.times.102 copies/mL) compared with the baseline (3.0.times.106 copies/mL; P <.05). After 12 mo, 8 of 24 (33%) patients had cleared HBV DNA and 12 (50%) had normal ALT levels. At the end of the study virol. and biochem. response was 50% and 21%, resp. Thus, virol. and biochem. response sustained in 5 of 24 (21%) patients retreated with ribavirin and IFN-.alpha.; none of them lost hepatitis B surface antigen (HBsAg). Liver histol. improved in 2 of 4 sustained responders but in none of the 12 nonresponders with paired biopsies (P =.05). The response was independent of dose and duration of previous treatment, viral load, or the distribution of HBV precore wild-type/mutant variants. However, sustained responders had significantly higher necroinflammation (P =.036) and fibrosis (P =.007) scores. IFN-.alpha.-related side effects were mild and reversible on discontinuation. In 4 (17%) patients who suffered nausea and diarrhea the ribavirin dosage was reduced by 50% after 1 mo of therapy and finally discontinued in all of them. No patient had liver disease decompensation. In summary, combination therapy with ribavirin and IFN-.alpha. may be efficacious to treat viremic anti-HBe-pos. patients with chronic hepatitis B who have failed previous IFN therapy.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:724912 CAPLUS
DOCUMENT NUMBER: 131:317484
TITLE: A preliminary study of long-term treatment with interferon gamma-1b and low-dose prednisolone in patients with idiopathic pulmonary fibrosis
AUTHOR(S): Ziesche, Rolf; Hofbauer, Elisabeth; Wittmann, Karin; Petkov, Ventzislav; Block, Lutz-Henning
CORPORATE SOURCE: Department of Internal Medicine IV, Division of Pulmonary Medicine, University of Vienna Medical School, Vienna, A-1090, Austria

SOURCE: New England Journal of Medicine (1999), 341(17), 1264-1269
CODEN: NEJMAG; ISSN: 0028-4793
PUBLISHER: Massachusetts Medical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Patients with idiopathic pulmonary fibrosis have progressive scarring of the lung and usually die within four to five years after symptoms develop. Treatment with oral glucocorticoids is often ineffective. We conducted an open, randomized trial of treatment with a combination of interferon gamma-1b, which has antifibrotic properties, and an oral glucocorticoid. We studied 18 patients with idiopathic pulmonary fibrosis who had not had responses to glucocorticoids or other immunosuppressive agents. Nine patients were treated for 12 mo with oral prednisolone alone (7.5 mg daily, which could be increased to 25 to 50 mg daily), and nine with a combination of 200 .mu.g of interferon gamma-1b (given three times per wk s.c.) and 7.5 mg of prednisolone (given once a day). All the patients completed the study. Lung function deteriorated in all nine patients in the group given prednisolone alone: total lung capacity decreased from a mean (.+-.SD) of 66.+-.8 percent of the predicted value at base line to 62.+-.6 percent at 12 mo. In contrast, in the group receiving interferon gamma-1b plus prednisolone, total lung capacity increased (from 70.+-.6 percent of the predicted value at base line to 79.+-.12 percent at 12 mo, P<0.001 for the difference between the groups). In the group that received interferon gamma-1b plus prednisolone, the partial pressure of arterial oxygen at rest increased from 65.+-.9 mm Hg at base line to 76.+-.8 mm Hg at 12 mo, whereas in the group that received prednisolone alone it decreased from 65.+-.6 to 62.+-.4 mm Hg (P<0.001 for the difference in the change from baseline values between the two groups); on maximal exertion, the value increased from 55.+-.6 to 65.+-.8 mm Hg in the group that received combined treatment and decreased from 55.+-.6 mm Hg to 52.+-.5 mm Hg in the group given prednisolone alone (P<0.001). The side effects of interferon gamma-1b, such as fever, chills, and muscle pain, subsided within the first 9 to 12 wk. In a preliminary study, 12 mo of treatment with interferon gamma-1b plus prednisolone was assocd. with substantial improvements in the condition of patients with idiopathic pulmonary fibrosis who had had no response to glucocorticoids alone.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:447938 CAPLUS
DOCUMENT NUMBER: 131:115063

TITLE: Retreatment of chronic hepatitis B e antigen-positive patients with recombinant interferon alfa-2a

AUTHOR(S): Carreno, Vicente; Marcellin, Patrick; Hadziyannis, Stephanos; Salmeron, Javier; Diago, Moises; Kitis, Geoge E.; Vafiadis, Irene; Schalm, Solko W.; Zahm, Friederike; Manzarbeitia, Felix; Jimenez, F. Javier; Quiroga, Juan Antonio

CORPORATE SOURCE: The European Concerted Action on Viral Hepatitis (EUROHEP), Department of Hepatology, Fundacion Jimenez Diaz, Madrid, 28040, Spain

SOURCE: Hepatology (Philadelphia) (1999), 30(1), 277-282
CODEN: HPTLD9; ISSN: 0270-9139

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fifty-seven patients with chronic hepatitis B, hepatitis B virus (HBV) e antigen (HBeAg) and HBV DNA positivity, and aminotransferase elevation despite a previous course of any type of adequate interferon alfa (IFN-.alpha.) therapy were included in a multicenter prospective randomized controlled trial. The objective of the study was to compare a second course of IFN-.alpha. therapy (9 million units [MU] of IFN-.alpha.-2a, Roferon-A, thrice weekly for 6 mo) vs. no therapy in terms of loss of HBV DNA and HBeAg. At the end of the study, a sustained clearance of HBV DNA and HBeAg was obsd. in 9 of the 27 (33.3%) patients who had received retreatment with IFN-.alpha. compared with 3/30 (10%) patients who spontaneously cleared these markers in the untreated control group ($X2 = 4.66$, $P = .031$; odds ratio: 4.5, 95%; confidence interval: 1.1-18.9). None of the responders lost HBsAg. Patients retreated with IFN-.alpha. were more likely to have biochem. remission in assocn. with HBV clearance (5/27, 18.5%) compared with untreated patients (1/30, 3.3%; Fisher's exact test $P = .09$). Histol. improvement in the liver necroinflammatory activity was obsd. among sustained responders to IFN-.alpha. retreatment, consisting of regression of the portal and periportal inflammation and of the piecemeal necrosis; there was no change in the degree of liver fibrosis. Side effects were similar to those previously reported during IFN-.alpha. treatment; these were mild and reversible on IFN-.alpha. discontinuation. None of the baseline features were assocd. with response by Cox's regression anal. In summary, viremic patients with chronic HBeAg-pos. hepatitis may experience disease remission following retreatment with IFN-.alpha.. Thus, retreatment with IFN-.alpha. may be considered a therapeutic option.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 32 OF 34 CAPLUS

ACCESSION NUMBER: 1997:624761 CAPLUS
DOCUMENT NUMBER: 127:277005
TITLE: Side effects of alpha interferon in chronic hepatitis C
AUTHOR(S): Dusheiko, Geoffrey
CORPORATE SOURCE: Royal Free Hospital and School of Medicine, London, UK
SOURCE: Hepatology (Philadelphia) (1997), 26(3, Suppl. 1), 112S-121S
CODEN: HPTLD9; ISSN: 0270-9139
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alpha interferons have been used widely to treat chronic hepatitis C virus infection. These include recombinant interferons, purified natural leukocyte, and lymphoblastoid interferons. Alpha interferon is administered by s.c. or i.m. injection either daily or three times weekly for a period of 6 to as long as 24 mo. A wide array of adverse effects of alpha interferon have been described. Several side effects such as fever, headache fatigue, arthralgias, and myalgias are common, esp. with the initial injections. These early side effects of interferon are predictable and are encountered in the majority of patients. These may not require dose modification, but can be problematic for a significant proportion of patients. Other adverse events effects may require dose modification or even discontinuation of therapy in 2% to 10% of patients. Neuropsychiatric side effects such as depression and irritability can be most troublesome; their mechanisms are not well understood. Granulocytes, platelets, and red blood cell counts decrease during treatment, but the decreases are usually mild, although they can be dose limiting if cell counts are low initially. Interferon has important immunomodulatory properties, and treatment can induce autoimmune phenomena, the most frequent being autoimmune thyroiditis with either hypothyroidism or hyperthyroidism, esp. in predisposed patients. Other autoimmune disease can be aggravated by interferon therapy. Severe and even life-threatening side effects of interferon occur in 0.1% to 1% of patients; these include thyroid, visual, auditory, renal, and cardiac impairment, and pulmonary interstitial fibrosis. Some of these side effects may be irreversible. Higher doses of interferon (above 5 million units three times weekly) cause higher rates of adverse events than std. doses. Contraindications to alpha interferon have been recognized.
REFERENCE COUNT: 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

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L31 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:397043 CAPLUS
DOCUMENT NUMBER: 127:134556
TITLE: Dose-response studies of interferon -.alpha.2b on liver fibrosis and cholestasis induced by biliary obstruction in rats
AUTHOR(S): Muriel, Pablo; Castro, Virginia
CORPORATE SOURCE: Departamento Farmacologia Toxicologia, Centro Investigacion Estudios Avanzados IPN, Mexico City, 07000, Mex.
SOURCE: Pharmacology (1997), 54(4), 179-185
CODEN: PHMGBN; ISSN: 0031-7012
PUBLISHER: Karger
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interferons were utilized widely in chronic liver diseases for their antiviral properties. There is evidence for their antifibrogenic actions. Effects were studied of various doses of interferon -.alpha.2b on exptl. liver fibrosis and cholestasis induced in the rat by biliary obstruction. Collagen was measured as hepatic hydroxyproline content. Cholestasis was detd. by serum alk. phosphatase and .gamma.-glutamyltranspeptidase activities and by bilirubin content. Glycogen was measured in the liver. The best effects (antifibrotic and anticholestatic) were obsd. in the group receiving the lowest dose of interferon. These results suggest that interferon -.alpha.2b may be used at low doses, thereby decreasing side effects and costs.

L31 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:542037 CAPLUS
DOCUMENT NUMBER: 125:213284
TITLE: Combination therapy with recombinant human erythropoietin, interferon-.alpha.-2b and granulocyte-macrophage colony-stimulating factor in idiopathic myelofibrosis
AUTHOR(S): Bourantas, Konstantinos L.; Tsiara, Stavroula; Christou, Leonidas; Repousis, Panagiotis; Konstantinidou, Pavlina; Bai, Maria; Seferiadis, Kostantin
CORPORATE SOURCE: Dep. Int. Med. Pathol. Biochem., Univ. Hosp., Univ. Ioannina Med. Sch., Ioannina, Greece
SOURCE: Acta Haematologica (1996), 96(2), 79-82
CODEN: ACHAAH; ISSN: 0001-5792
PUBLISHER: Karger

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Seven patients, 3 men or 4 women 48-72 yr of age and suffering from idiopathic myelofibrosis were given a combination of recombinant human erythropoietin (r-hu-Epo), interferon-.alpha.-2b (IFN) and GM-CSF, to treat their pancytopenia and marrow fibrosis. The dose of r-hu-Epo was 200 U/kg 3 times weekly, that of IFN was 3.times.106/U 3 times weekly, and that of GM-CSF was 250 .mu.g/m2/daily. The duration of therapy ranged from 3 to 6 mo for r-hu-Epo and IFN and was 3 wk for GM-CSF. The treatment regimen has a beneficial effect on all patients. The levels of Hb increased in all patients but particularly in 5 (2 of whom had been dependent on red blood cell transfusions). Splenomegaly decreased significantly in 4 patients. Fibrosis in the bone marrow decreased in 2 patients. Three patients also had an increase in the no. of white blood cells during the therapy with GM-CSF. The authors obsd. mild side effects in 6 of the patients. One patient had severe side effects from IFN and treatment was discontinued. In conclusion, the combination of r-hu-Epo, IFN and GM-CSF may improve the anemia (due to r-hu-Epo), increase the white blood cell count (due to GM-CSF) and reduce the marrow fibrosis (probably due to IFN) in patients with idiopathic myelofibrosis.